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THE TREATMENT OF CARCINOMA OF THE CERVIX DURING PREGNANCY

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THE treatment of carcinoma of the cervix occurring during pregnancy is complicated by the conflicting facts that radium irradiation is the most trustworthy method of therapy for carcinoma of the cervix, but can damage the developing fetus, especially when used in the early months of gestation. Because of this danger to the child, many observers have concluded that irradiation in any form or dosage is contraindicated, so long as the pregnancy is allowed to continue. Leopold Goldstein and Douglas Murphy[1] in a series of papers in 1928 and 1929 brought together the existing literature, which clearly demonstrated that therapeutic pelvic irradiation during pregnancy is extremely likely to injure the growing fetus and that such injury may result in the birth of a seriously defective child; in 75 instances of irradiation during pregnancy, there was an uncorrected figure of 50.7 per cent defective children. However, a closer analysis of the data reveals extenuating circumstances in many cases; for example, in some instances substantial high voltage roentgen dosage was delivered to a pregnant uterus in the mistaken belief that it was a myoma. This fact, along with our own and the varying experiences of others with cervical cancer, has led us to believe that the conclusion of Goldstein and Murphy, while indicating the danger of irradiation during pregnancy, does not necessarily outweigh its advantage in treating carcinoma of the cervix.

Contributors to the literature have resolved themselves into two principle groups—those who do not permit irradiation of cervix cancer if pregnancy is allowed to continue, and those who feel that properly applied radium irradiation is justifiable and safe. Either point of view

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is often supported by a single case report issued almost before the patient leaves the hospital so that an estimation of the five-year salvage, or the ultimate outcome for the baby is impossible. There are well over 200 references to this subject in the *Quarterly Cumulative Index Medicus,* but scarcely more than a dozen reports that fulfill the essential requirement of an elapsed time of five years so necessary in a discussion of carcinoma. Thus, many reports are invalid in a discussion of the results of treatment in carcinoma of the cervix, and are also worthless from the standpoint of prognosis for the infant, as it is well known that one of the most serious deformities caused by irradiation, microcephaly, is often not recognizable at birth. A period of about three years must elapse before one can be sure that this distressing condition does not exist.

Our own experience with carcinoma of the cervix during pregnancy, and a study of the reported cases, in so far as they are helpful, has led us to believe that the treatment of such patients must be individualized; one general rule of therapy, which either allows radiation and continuation of pregnancy, or dictates interruption of the pregnancy as a necessary part of the treatment is not applicable. If there is a probability of obtaining a normal child in treated cases, and if the circumstances of the case so justify it, the attending physician must indicate this possibility to the patient. In a multipara with adequate family, it would be unwise to assume even a slight hazard of fetal injury, provided interruption of the pregnancy will not endanger the prognosis for the mother. Many patients pregnant for the first time would desire to entertain a reasonable risk of an abnormal baby, if their own chance of cure was not compromised.

Our problem therefore, is to estimate the risk of an abnormal fetus following irradiation for carcinoma of the cervix during pregnancy, and to examine the prognosis for the mother with and without interruption.

The Risk of Fetal Abnormality Following Radium Irradiation for Carcinoma of the Cervix

In order to estimate the risk of fetal damage with radium in the treatment of cervix cancer during pregnancy, we have collected all cases of this condition and added our own experience. This material is summarized in Tables I and II. Some of the cases herein reported were previously described by Neill[2] but are included with additional follow-up notes.

There are 48 cases, exclusive of our own, in which irradiation was used sometime following conception and prior to delivery.

One may arbitrarily set three years as the time which must elapse in order to be sure about the occurrence of microcephaly. There are reported only seven normal children which fulfill these requirements.

There are 28 indeterminate cases, that is, cases reported prior to three years after delivery. Practically all of these children are quoted as normal.

There are five examples of abnormal offspring. Two of these five treated many years ago, received x-ray therapy and therefore should be excluded. Two are macerated fetuses. One of these two was irradiated at 4 months and the other at 3; both went almost to term. There remains but a single reported case prior to our own of a living child with microcephaly following radium treatment for carcinoma of the cervix. This patient was treated at 6 months, and both patient and child were living 11 years at the time of the report.

There are also eight reported cases of neonatal deaths due to incidental causes such as measles, pyloric obstruction and pneumonia.

Our own material (Table II and Case Reports) includes 8 instances of prenatal irradiation. There are five children living and normal from three to fifteen years of age. There are two instances of microcephaly, but one of these contracted tuberculosis and died at the age of four years. There is one child who seemed normal in every way, but who died of measles at the age of 18 months.

Combining our own material and the literature, there are twelve children irradiated prenatally who are living and normal more than three years of age. There are 28 children living and apparently normal but reported before three years. There are nine children who died of some unrelated disease before three years. There are three cases of microcephaly.

It is difficult, due to limitation of numbers, to express the risk of microcephaly percentage-wise. If only determinate cases are considered, there are three seriously abnormal children in a total of 15 live births, or 20 per cent. If the entire group is considered, the figure would be three in fifty-two, or 6 per cent.

Five months is sometimes cited as the earliest time at which irradiation should be applied. At that time the fetus is higher in the abdomen, thus affording greater distance from the source of irradiation. There is also said to be less likelihood of abortion, if ovarian function be destroyed at that time. There is little real evidence to support such view although it may well be correct. Of the 48 reported cases, 8 were treated prior to five months. Two of these went to term and delivered macerated fetuses. One is living and well at eight years. Five are said to be living and well, but under three years of age. There are 40 reported cases treated later than 5 months. These yielded 6 children living and normal more than 3 years after delivery, 23 living and normal but reported prior to 3 years of age, 8 children dead of undetermined causes and 3 abnormal children. Two of these last three were treated with high voltage roentgen therapy and can be eliminated for our purposes; the third one treated at 6 months is a living microcephalic 11 years of age at time of report.

Three of our cases were treated prior to 5 months. Two of these were microcephalic, one of which is still living at 3½ years of age. Five were treated after 5 months, and none of these developed microcephaly.

TABLE I

AUTHOR	AGE	DURATION OF PREGNANCY	CLINICAL STAGE	IRRADIATION	DELIVERY	END RESULT MOTHER	END RESULT CHILD
Mundell[3]	33	25 weeks	I	1,800 mg. h. each week for 3 weeks 6/12/38	Cesarean section 9/15/38	Living under five years 4/18/39	Living and normal 4/18/39
Herold, K.[4]	(?)	5 months		Radium	Spontaneous		Normal
Hoffmann, H.[5]	(?)	5 months		Radium	Spontaneous		Normal
Pouey,[6]	34	6½ months	II	11/28/23—43.2 mc. d. in 8 days	Spontaneous 20 hours labor	Living under five years 5/1/27	Living and normal 5/1/27, more than 3 years
Couvelaire,[7]	(?)	5 months		Radium	Cesarean section 8½ months		Normal
Condamine, R.[7]	38	5 months		Radium	Spontaneous		Normal
Titus,[3]	(?)	5 months		Radium	Spontaneous		Normal
Brouha, M., and Gosselin, O.[8]	31	7 months	I	48 mc. d. in 10 days 1800 x 4 post-partum	Cesarean section plus panhys-terectomy	Died 18 months, recurrence in broad ligament	Pyloric stenosis. Died from operation
Berkley, C.[9]	34	26 weeks	I or II	3,600 mg. h.	Cesarean section plus Wertheim	Living and well 20 years	Living and normal 20 years
Van Rooy, A. W.[10]	41	4 months	I	4,200 mg. h. 6/9/33	Spontaneous 1/10/34	Well under 5 years	Well under 3 years
Paroli, G.[11]	29	3 months		Radium			Living and normal
Zimmerman, R.[12]	33	5 months		Radium			Living and normal

Amico-Roxas, S.[13]	27	6 months		Radium	Cesarean section and hysterectomy		
Fagioli, M.[14]	28	6 months		Radium	Cesarean section		
Smith, F. R.[15]	36	6½ months	"Early"	Radium	Cesarean section 8 months	Died 18 months	Died 3 days; atelectasis
Petenyi, G.[16]	(?)	5 to 7 months		X-ray	Spontaneous		Microcephaly and eye damage
Gol, F.[17]	(?)			X-ray	Spontaneous		Microcephaly
Goldstein, L., and Murphy, D. P.[1]	29	6 months	II "Schmitz"	185 mg. for 24 hours, May, 1916	Spontaneous 6/21/16	Living and well 11 years	Microcephaly 11 years
Schilling, N.[18]	32	"Advanced"	I	100 mg. for 24 hours	Cesarean section 3/23/23	Died postoperative	Died 3 hours
Strauss, A.[19]	38	5 months	"Operable"	3,000 mg. h.	Cesarean section plus panhysterectomy	Died 2 years; recurrence	Died soon after delivery
Metzger and Leguen[20]	31	3 months	I	18 mc. d.	Forceps	Died of recurrence 18 months	Living and normal 20 months
Hartman, H., and Farber, S.[21]	35	4 months	II	32.9 mc. d.	Cesarean section and supravaginal hysterectomy	Living with growth 2 months	Living and normal 2 months
Roy,[22]	29	4 months		47 mc. d. in 5 months	Spontaneous	Died	Died 10 days
Condamine, R.[23]	25	1½ months		Radium	Spontaneous	Died from laceration of cervix after delivery	Died from difficult delivery

TABLE I—CONT'D

AUTHOR	AGE	DURATION OF PREGNANCY	CLINICAL STAGE	IRRADIATION	DELIVERY	END RESULT MOTHER	END RESULT CHILD
McGlinn, J. A.[24]	31	3 months		24 mc. d.	Spontaneous	Died 9 months	Macerated at birth
Heuze,[25]	39	4 months		40 mc. d.	Cesarean section	Living and well 6 years	Living and normal 6 years
Karg, C.[26]	30	6 months	"Early"	55 mg. for 24 hours	Spontaneous	Died 1 year	Living and normal 8 years
Bottaro, and Mengoa,[8]	(?)	16 months		50 mg. for 24 hours repeated 5 times in 8 days	Cesarean section at term		
Field, C. E.[27]	39	6 months	II	7,230 mg. h. March 3 to 26, 1919	Spontaneous 4/26/19	Died 6/17/20	Living and well 3 years
Bailley, H., and Bagg, H. J.[28]	35	6½ months		3,613 mg. h.	Cesarean section at term 4/3/20	Died of eclampsia 4/16/20	Normal; died of pneumonia 2½ months
Cathala and Mérat[29]	35	7 months		Radium	Cesarean section and hysterectomy 3 days after radium treatment	Died postoperative	Living under 3 years
Garipuy, R.[30]	42	7 months		100 mg. for 72 hours	Spontaneous	Living and well 10 months	Living and normal 10 months
Karg, C.[26]	33	8 months		55 mg. for 24 hours	Spontaneous	Living and well 1 year	Living and normal 1 year
Heurotey and Cheval[31]	35	8 months		68 mc. d. 15 days	Cesarean section and hysterectomy at term	Living	Living

Porte and deNabias[32]	36	5½ months		32 mc. d.	Cesarean section 8½ months	Living and well 1 year	Living and normal 1 year
Hauch, E.[33]	36	9 months		Radium	Cesarean section and hysterectomy	Died 4 days post-operative	Living and normal
Godlewski, E.[34]	(?)	7 months		Radium	Cesarean section and hysterectomy 8 months	Died with metastases	Living
Roy[22]	28	7 months		27.5 mc. d. 5 days	Cesarean section and hysterectomy		Normal
Roy[22]	36	7 months		Radium	Cesarean section at term	Died	Normal
Condamine, R., Voron and Molin[23]	38	5 months		25 mc. d.	Spontaneous	Living and well 3 months	Died 1 month
Infantizzi[8]	(?)	7 months		Radium	Spontaneous		Living
Belle[88]	38	5 months		40 mc. d.	Spontaneous	Died 1 year	Living and normal
Döderlein, A.[35]	33	7 months		2,440 mg. h.	Spontaneous	Died 2 years	Living and normal 3 years
Döderlein, A.[35]	30	7 months	Extensive	2,440 mg. h. x 3	Spontaneous	Died 1 year	Living and normal 9 years
Kirtz, L. P., and Pareira, M. D.[36]	32	7 months	I	3,350 mg. h.	Cesarean section	Living under 5 years	Living and normal 3 years

Our own material more than the literature tends to support the opinion that irradiation is much safer for the fetus, if used after 5 months. We are, therefore, greatly influenced by the duration of gestation in recommending treatment.

At times abortion occurs from 1 to 60 days following the application of radium to the cervix, and there are about 15 such cases reported: about half of these were treated before the pregnancy had progressed five months. It is likely that many more such cases have never been reported. Manipulation of the cervix incident to the treatment could be more responsible for abortion than injury to the child, or destruction of ovarian function.

Dosage of radium is important, but none of the cases with abnormal fetuses received excessive treatment considering the growth. Furthermore, normal children were born to mothers who received as much or higher dosage. It was impossible in our own cases to correlate in any way dosage estimated to be delivered in the region of the child's head with the occurrence of microcephaly.

Risk to the Mother

An estimation of the possible risk which the mother may suffer from the interruption or continuation of the pregnancy is essential in planning treatment. This figure can best be determined by a study of comparable series treated on one hand by irradiation and continuation of pregnancy, and on the other by irradiation with interruption of pregnancy. In discussing the risk to the child, it was pointed out that case reports were issued too soon to be of real value in determining the health of the child; this is likewise true in determining the ultimate outcome for the mother.

In the treated uninterrupted cases (Table I), there are only three mothers living and well more than five years. There are 18 mothers dead, most of these within the first 18 months following treatment. In 24 instances reports of living mothers were issued prior to five years following treatment.

Our own results (Table II) show seven mothers treated during eight pregnancies. Two are dead, one is living at three years, and four mothers treated during five pregnancies are living and well five years or more after treatment.

Unsatisfactory as are these figures, the number of published cases treated with radium plus abortion either spontaneous or induced, is even more meager. Phillipp[37] has reported a case living seven years. She was treated at four months and had a spontaneous abortion at 6½ months. Danforth[38] reports a case well for seven years in whom a very early pregnancy was curetted from the uterus just prior to inserting the radium. On the other hand, there are at least two reported cases (Moris,[39] Danforth[38]) of instrumental abortion followed by death from infection. Most of the case reports are issued far too soon for an

TABLE II

NAME	AGE	DURATION OF PREGNANCY	CLINICAL STAGE	TREATMENT		DELIVERY	FOLLOW-UP MOTHER	FOLLOW-UP BABY	POST-PARTUM TREATMENT
O. H.* 17355	28	6 months	II	12/18/26	1,762 mc. h.	1/16/27 Cesarean section	Died met. Sept., 1930	Living and normal, 3/31/42	2/12/30—500 mc. h.
M. B.* 22599	32	5 months	II	5/13/30	3,109 mc. h.	9/12/30 Cesarean section	Living and well, 1942	Living and normal, 1942	
A. W.* 24792	29	6 months	I	11/28/31 1/ 9/32	2,671 mc. h. 843 mc. h.	2/11/32 Cesarean section	Living and well, 1943	Living and normal, 1943	
S. B. 30042	30	7 months	I	2/23/36	2,940 mc. h.	6/19/36 Cesarean section	Living and well, 1943	Living and normal, 1943	
H. S. 31471	35	6 months	I	4/16/37	1,614 mc. h.	6/24/37 Cesarean section	Living and well, 1943	Died 18 months Measles	
H. S. 31471	36	4 months	I	2/10/38	3,204 mc. h.	7/19/37 Cesarean section	Living and well, 1943	Microcephaly Died tuberculosis, 8/4/42	
M. L. 33975	33	4 months	I	2/25/39 3/ 4/39 4/ 2/39	1,752 mc. h. 1,001 mc. h. 1,169 mc. h.	6/4/39 Cesarean section	Died July, 1941—recurrence	Microcephaly	2/13/40—690 mc. h. plus 2,000 r. times 4
J. H. 34894	38	4 months	I	10/12/39 10/16/39 10/23/39 11/13/39	1,072 mc. h. 1,064 mc. h. 506 mc. h. 618 mc. h.	Jan., 1940 Cesarean section	Living 3/12/43	Living and normal, 3/12/43	

*Previously reported by Neill.[2] AM. J. OBST. & GYNEC. 30: 414, 1935.

estimation of the cure rate. There are also probably many cases with spontaneous abortion following treatment which have not found their way into the literature.

These considerations make it impossible to estimate statistically the relative merits and dangers of abortion in the treatment of cervix cancer. It is certain however, that continuation of the pregnancy by no means precludes a cure as indicated by the literature and our own experience. The influence of pregnancy on tumors in general is problematical. The alteration in circulation contingent upon the interruption of pregnancy may exert an unfavorable influence in curing the cervical growth; this possibility is suggested by the very poor prognosis in cases treated at term by necessity with cesarean section, before the treatment of the cervix cancer. It is only fair to say however, that in this latter group the cases are generally more advanced than those seen earlier in pregnancy.

In this discussion very little has been said about the extent of disease in relation to cure. Obviously, this consideration is as important here as in uncomplicated cervix carcinoma. The number of reported cases is too few to make such a correlation of significance. It is to be noted that the majority of prenatal cases is not more advanced than League of Nations Stage II. The neglected extensive cases are not encountered until term when delivery of the child is imperative. In estimating the proper therapeutic procedure in a particular case, due weight must be given to the clinical stage of the disease. One would hesitate to accept for treatment with a view to carrying to term a patient with disease more extensive than Stage II. Because of the pregnancy with its attendant examination most cases will be discovered relatively early.

Technique of Treatment

If it is decided to treat during pregnancy with a view to obtaining a normal living child at term, certain points in technique may be stressed. It is important that no high voltage roentgen-ray therapy be employed because of the obvious dangers of substantial depth dosage in the region of the developing child. Furthermore, it has been our practice to omit the use of tubes within the cervical canal. This is done for the twofold purpose of securing all possible distance from the baby and also to guard against the onset of labor by dilating the cervix. The entire treatment is carried out by tubes held in a cloth plaque against the cervix. The details of treatment in uncomplicated cervix cancer have been previously described.[40] As an additional precaution against stimulating uterine contractions by prolonged packing against the cervix, we have preferred to use a large amount of radium for a correspondingly short period of time. This means the use of 2.5 to 3 grams of radium. While it is by no means necessary to have available such a quantity of radium for the successful treatment of these cases, the fact that we

have in no case stimulated uterine contractions leads us to believe that this is not an unimportant point.

The dosage is subject to more variation than in uncomplicated cervix carcinoma. This variation is allowable in an effort to spare the fetus all possible treatment and must be determined by clinical experience. In the cases herein reported, the dose varied from 1,614 mc. hr. to 3,922 millicurie hours.

Following delivery it is often desirable to administer additional radium and x-ray.

Operative Treatment

Irradiation is by far the most common method of treatment for uncomplicated carcinoma of the cervix. In spite of this, many cases complicated by pregnancy have been treated by panhysterectomy. This is probably because panhysterectomy seems expedient if abdominal section for delivery of the child is necessary. Nevertheless, one should be hesitant in accepting this as a suitable method of therapy in view of the unsatisfactory results from panhysterectomy in uncomplicated cervix carcinoma even in carefully selected material.[41]

The reported cases based on this method are too few to express the cure rate statistically, but Newell and Scrivner,[42] Stacey and Thompson,[43] Stoekl,[44] Miller,[45] Chalfont,[46] Biro[47] and many others have reported such cases both at term and before with an alarmingly high operative mortality. Furthermore, most of these reports have appeared before an elapsed time of five years so that an estimation of carcinoma of cervix curability is not possible. In our opinion, any necessary abdominal operation either before or following irradiation of cervix carcinoma should be confined to evacuation of the uterus.

Pregnancy at Term

If the baby is viable when the carcinoma is discovered, the problem of injury to the fetus by irradiation need not be considered. Under these circumstances, the child can and often must be delivered by cesarean section. The prognosis under these circumstances has been very poor. There are approximately 40 reported cases to which we have added four treated by various methods including irradiation, panhysterectomy or both; as far as we are aware, the two cases reported by Biro[47] are the only ones which have survived more than five years. The poor prognosis was in many instances due to the advanced stage of the growth. However, the profound circulatory changes following parturition may be an unfavorable influence in arresting the disease.

The impression received from reviewing the cases of this group, emphasized by the experience of our own four cases, is of a lost opportunity on the part of the attending physician to diagnose and treat an early carcinoma. Almost without exception, the possibility of making an early diagnosis was dissipated by failure to use such simple diagnostic

procedures as speculum examination and biopsy even after the appearance of such an alarming sign as slight vaginal bleeding during pregnancy. Prenatal care through its routine periodic examinations offers an unequaled opportunity to diagnose carcinoma of the cervix at an early stage.

Summary and Conclusions

In formulating a plan for a clinical situation as rare as the association of pregnancy and carcinoma of cervix, one must draw upon the collective experience of the literature as well as upon one's own cases. It is therefore to be regretted that in so many instances, case reports have been issued too soon to be of value in estimating the ultimate outcome either for mother or baby. Many more detailed reports of this condition are needed, but these should not be published before the patient has died, or five years after treatment has elapsed.

We have come to believe that a general rule for the handling of these cases must take into account the obstetric and social background as expressed in the desire of the prospective parents for the child, as well as the extent of the disease. If there are other children, or if the parents do not care to assume the ever present risk of an abnormal child, we see no reason to advise any course except interruption of the pregnancy and adequate irradiation therapy.

The risk of an abnormal fetus cannot be statistically stated at the present time with certainty, but it seems probable that its upper limit is 20 per cent. If the parents and physician for any reason wish to assume this risk, it is justifiable, in our opinion, to proceed with irradiation during pregnancy with a view to obtaining a living child at term. If the pregnancy is at the fifth month or beyond, the risk of an abnormal child is substantially less. As indicated above, the risk to the mother is probably not increased by this procedure as compared with interruption of the pregnancy. The mother's prognosis is intimately related to the clinical extent of the disease. The general experience has been that most cases are discovered early (League of Nations I or II), and the prognosis has been parallel but somewhat lower than for corresponding but uncomplicated groups.

The prognosis of carcinoma diagnosed at term and treated by cesarean section plus panhysterectomy or irradiation, is grave. This is in a large measure due to failure of the attending physician to suspect the diagnosis and apply such simple clinical methods as speculum examination and biopsy, even in the presence of vaginal bleeding during pregnancy.

Case Reports

CASE 1.—O. H., 17355, aged 28, four living children, youngest 3 years. Had irregular vaginal spotting for 3 months. Did not remember missing any periods, but on examination December 18, 1926, she was estimated to be 6 months pregnant. At another hospital, it was thought

that she had a small cervical fibroid which was removed 12/1/26. Pathologic examination however, showed squamous-cell epithelioma. At the examination December 18, the entire cervix was involved and there was some extension of the growth on the vaginal wall. No parametrial extension by rectal examination.

Treatment: 12/18/26—2,644 mc. against the cervix by 7-tube plaque for 40 minutes. Patient went into labor spontaneously 1/16/27 and was delivered by cesarean section. Patient got along very well until 1930, when there was a recurrence. In spite of further treatment with radium and x-ray, the patient died September 12, 1930, from the disease. Female child was examined March 31, 1942, and found to be normal in every way. She was above average in her school work.

CASE 2.—C. B., 22599, aged 32, 3 living children. L. M. P. 12/16/29. Three months prior to May, 1930, there was irregular bleeding and discharge. On examination 5/13/30, it was estimated that she was 5 to 6 months pregnant. On the anterior lip of the cervix, principally on the left side, there was a hard growth. It extended somewhat on to the vaginal wall. Rectal examination showed that there was some induration in the right broad ligament. Biopsy revealed squamous-cell carcinoma.

Treatment: 5/13/30—3,109 mc. by 7-tube plaque against the cervix for one hour. Pregnancy progressed normally and the cervix healed. On September 12, 1930, she was delivered by cesarean section. At operation, the broad ligaments were carefully palpated, and no mass could be felt. Following delivery, there was a recurrence of the normal menstrual flow which was abolished by x-ray in June, 1931. Patient has been examined at intervals since then, the last time being June 12, 1942, at which time she was well. The female child was also examined June 12, 1942, and found to be normal in every respect. She was doing well in her school work.

CASE 3.—A. W., 24792, aged 29. Four normal pregnancies during the last six years. All children living. Patient has never menstruated between pregnancies. In January, 1931, had some spotty vaginal bleeding. There was a little staining each day. In September, 1931, she bled rather profusely for 5 days. First seen November 23, 1931. Abdominal examination showed pregnancy which was estimated to be between six and seven months. Vaginal examination revealed a friable mass confined to the posterior lip of the cervix with no extension on to the vaginal wall. Rectal examination demonstrated no parametrial involvement. Biopsy showed squamous-cell carcinoma.

Treatment: On November 28, 1931, the patient received a 7-tube plaque containing 952 mc. against the cervix for one hour. She was given also four permanent gold radon implants for a total of 20.6 mc. On January 9, 1932, patient received a 5-tube plaque containing 1,606 mc. for 30 minutes. The regression was very satisfactory. On February 11, 1932, a classical cesarean section was performed. At the time of operation no mass could be palpated in the broad ligament region. Since operation, the patient has had no further treatment and is well as of November 1, 1941. The female child was also examined on that date and was normal and getting along in school better than the average for her age.

CASE 4.—S. B., 30042, aged 30. Nine pregnancies and five living children. L. M. P. stated to be October 1, 1935; however, at the time of

examination, February 23, 1936, it was estimated that she was 7 months pregnant. On February 9, she first noted a slight bloody discharge and on February 12, had rather severe bleeding. On the anterior lip of the cervix there was a granular ulcer. There was little or no extension on to the vaginal vault. The posterior lip of the cervix seemed normal. Rectal examination revealed no apparent extension into the broad ligaments. Biopsy showed squamous-cell carcinoma.

Treatment: 1,960 mc. divided into 1 tube in the cervical canal and a 5-tube plaque against the cervix for 1½ hours. Following this, the lesion healed and on April 30, 1936, the cervix appeared grossly normal. On June 5, 1936, a female child was delivered by classical cesarean section. March 12, 1943, mother alive and well, and child living and normal, walked at 11 months.

CASE 5.—H. S., 31471, aged 35, five previous pregnancies; 5 living children. L. M. P. October 8, 1936. First noticed vaginal spotting in the latter part of March, 1937. Never had any irregular bleeding prior to this time. Lost 8 pounds in weight. Examination showed a pregnancy estimated to be 5 months. On the left side of the cervix, there was an ulcer about 2 cm. in diameter. No extension on to the vaginal wall. No involvement of the parametria. Biopsy showed squamous-cell carcinoma of the cervix.

Treatment: On April 16, 1937, received 2,150 mc. against the cervix with a 5-tube plaque for ¾ of an hour. Following the treatment, there was rapid healing of the lesion. Cesarean section on June 24, 1937. Following delivery, it was noted that there was some induration of the right side of the cervix. The patient was given an appointment to report back for further treatment but was very slow in doing so and in February, 1938, when she reported for examination, she was found to be again four months pregnant. Biopsy again showed squamous-cell carcinoma which involved the entire cervix but had not involved the vaginal walls or the parametria. On February 10, 1938, she received 2,746 mc. against the cervix for 1 hour and 10 minutes. For a second time, there was a rapid healing of the lesion and at term a second cesarean section was done. She has been followed at intervals since that time, and there has been no recurrence of the growth. The first child died at the age of 18 months. It was in good health until it contracted measles and died. The second child was mentally defective. She entered the Polk (Pa.) State School May 19, 1942. She was classed as an imbecile with an I.Q. of 43. Soon after admission, she showed evidence of active tuberculosis and died August 4, 1942.

CASE 6.—J. H., 34894, aged 38. Four previous pregnancies, the last one 10 years ago. All children living and well. First seen October 12, 1939. Patient complained of intermenstrual bleeding of one year's duration. She was estimated to have a pregnancy of four months. The right side of the cervix was involved in a growth, biopsy of which showed squamous-cell carcinoma. The left side of the cervix was normal, and there was no spread on to the vaginal mucosa or into the parametria.

Treatment: 10/12/39, 1,072 mc. for one hour. 10/16/39, 1,847 mc. against the cervix for 35 minutes. 10/23/39, 1,012 mc. against the cervix for 30 minutes. 11/13/39, 1,236 mc. against the cervix for 30 minutes. There was improvement in the lesion and the patient had a cesarean section in January, 1940. On March 12, 1943, the mother was alive and well, and the child was normal.

CASE 7.—M. L., 33975, aged 33. Patient has 8 living children. L. M. P. October, 1938. First seen February 25, 1939. Examination February 25, 1939, showed a pregnancy which was estimated to be four months. There was a granular growth involving the posterior lip of the cervix and cervical canal. The anterior lip was also thought to be involved as it was stony hard although the overlying mucous membrane appeared normal. Rectal examination showed no involvement of the parametrium.

Treatment: February 25, 1939, 2,628 mc. divided into tube in cervical canal and a 5-tube plaque against the cervix for 40 minutes. 3/4/39, 2,003 mc. similar set up for 30 minutes. 4/2/39, 2,338 mc. with a plaque against the cervix for 30 minutes. Cesarean section June 3, 1939. Careful palpation of the parametrium at the time of operation revealed no induration. The baby appeared grossly normal. There was a recurrence of the growth in November, 1939, and she received a course of x-ray therapy of 8,000 r. through six portals around the pelvis (250 k.v. 30 Ma. 1 mm. copper plus 1 mm. aluminum—15 by 10 portals; 50 cm. S. T. D.; r. measured with scattering). She also received 1,380 mc. for 30 minutes against the cervix. However, she did not do well and died in July, 1941, from the disease. The baby was examined several times and was found to be mentally deficient. By March. 1943, she was not able to talk.

CASE 8.—T. K., 23125, aged 35. August 24, 1930, had normal spontaneous delivery. This was the tenth child. There had been some bleeding during the latter part of the pregnancy. Examination September 23, 1930, revealed the entire vault of the vagina to be filled with a large growth. There was extension into both broad ligament regions but no firm fixation. Biopsy showed squamous-cell carcinoma.

Treatment: October 4, 1930, 3,660 mc. 2 tubes in cervical canal and a 5-tube plaque against cervix for 50 minutes. There was some improvement, but patient died of the disease in July, 1934, in spite of subsequent treatment with x-ray and radium.

CASE 9.—M. H., 24229, aged 38. Multipara 3-0-1-2. L. M. P. September 15, 1930. Pregnancy was normal until February 22, 1931, when she began to bleed in small amounts. Examination June 5, 1931, showed pregnancy of 8½ months' duration. There was a nodular cervix with a growth confined entirely to the portio vaginalis. Biopsy revealed squamous-cell carcinoma. The broad ligaments seemed to be free. As the child was viable, immediate cesarean section was advised and carried out on June 6, 1931. Patient did not receive radium treatment until July 12, 1931. At that time there had been some increase in the size of the growth which was still limited to the cervix. The fornices were clear. There did seem to be some thickening of the right broad ligament region, although at the time of the cesarean section, careful palpation did not reveal any involvement of the broad ligament regions.

Treatment: July 12, 1931, 1,498 mc. for 2 hours with a seven-tube plaque against the cervix.

X-ray 7/16/31, 1,000 r. 7 by 7 suprapubic portal.
7/23/31, 1,000 r. 7 by 7 right lateral and left lateral pubic and 1,000 r. on perineal portal.
7/30/31, 10 by 10 portal 1,000 r. right lateral sacral and 1,000 r. left lateral sacral. Factors as in Case 7.

There was improvement but on September 30, 1931, there was still an ulceration 1½ cm. in diameter which on biopsy showed active growth. Two gold points each containing 6.8 mc. of radon were inserted into this area. On November 1, 1931, patient received 1,060 mc. in the cervical canal for 57 minutes. Patient did not improve and she died of the disease on April 23, 1932.

CASE 10.—E. F., 24280, aged 39. Patient has had 6 children and two miscarriages. All children living. At term the patient had a cesarean section on December 10, 1929, at another hospital. Apparently, it was a classical cesarean section and a supravaginal hysterectomy. It was not until July 25, 1931, that she came under our observation. There had been no bleeding from the time of the cesarean section until May, when it recurred and has continued to the time of examination. A large mass protruded from the cervix and extended on to the vaginal wall. Both parametria were involved to the pelvic wall, and there was fixation to the rectum. It was a very extensive case.

Treatment: July 25 and 26, received 1,000 r. of x-ray through 10 by 10 portals, 9 fields around the pelvis. Factors as in Case 7. August 3, 1931, received 2,673 mc. in and on the cervix for 67 minutes. On August 17, 1931, she died rather suddenly.

CASE 11.—M. K., 34297, aged 31. First seen May 11, 1939. Eight months previously patient had had a cesarean section because of an undilatable cervix. After several hours in labor, there was no progress and section was decided upon. Following this, there continued to be some vaginal discharge until the diagnosis of carcinoma of cervix was made. At this time, the growth was rather massive and had spread into both parametrial regions. Treatment was begun by x-ray and she received 8,000 r. through four portals from May 9, 1939, to May 18, 1939. Factors as in Case 7. On June 1, 1939, 1,212 mc. in and on the cervix for 1 hour. June 22, 1939. 2,361 mc. on the cervix for 35 minutes. Following this, she received many other radium and x-ray treatments, but the growth could not be cured, and she died August 15, 1941.

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OBSERVATIONS ON THE RH-FACTOR IN ITS RELATION TO HEMOLYTIC ANEMIA OF THE NEWBORN INFANT*

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THE work of Levine and his associates[1-3] has established the role of the Rh-factor in the pathogenesis of erythroblastosis fetalis. In view of the fact that there still remain problems which have not yet been clarified, the publication of further observations appears justifiable. In agreement with Kariher and Spindler,[4] Smith[5] and others, it would appear desirable to abandon the previous terminology such as erythroblastosis fetalis, icterus gravis, congenital anemia and hydrops fetalis which designate some of the clinical manifestations associated with the disease. Since hemolytic anemia is the most important feature the terms, "anemia hemolytica neonatorum, or hemolytic anemia of the newborn," seem appropriate for all forms of the disease. For the sake of brevity it will be represented by the abbreviation, HAN, in this paper.

During the past year, six cases have been investigated from clinical and serological points of view. Because they introduce a number of interesting questions for consideration, they will be described in some detail.

Case Reports

CASE 1.—(Ba.) This mother had five pregnancies. The first child was born in 1937, and is well. The second, born in 1939, had jaundice for the first ten days of life. A red cell count was 4.3 million and hemoglobin, 87 per cent on the third day. These were 5.6 million and 95 per cent respectively, two days later. The liver was slightly enlarged. This child is now well. The third pregnancy, in 1941, resulted in the delivery of a living full-term male infant who died after three hours. Autopsy revealed a ruptured spleen. No jaundice was observed during life or at autopsy. The liver was enlarged. Microscopic sections of the spleen showed hematopoiesis suggestive of HAN. The fourth pregnancy, in 1942, and the fifth, in 1943, both terminated with spontaneous expulsion of a macerated fetus of about five months' gestation. No microscopic study of organs was possible. Blood grouping† of the living members of the family after the last miscarriage was as follows:

	Group	*Rh*
Father	A	+
Mother	B	-
Son	A	+
Daughter	AB	+

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†The technical procedure employed for the determination of Rh constitution was that recommended by the Blood Transfusion Association of New York, in the pamphlet, "Instructions concerning the use of human anti-Rh serum."

The serum of the mother tested against several samples of Rh-positive and Rh-negative red cells demonstrated the presence of anti-Rh agglutinins. Tests for α agglutinins revealed a titer of 1:1,024. Two months later, the findings were the same. After four months only traces of anti-Rh agglutinins could be found and the titer of α agglutinins fell to 1:128.

CASE 2.—(Fr.) This mother had one normal living child. Two and a half years later, in 1943, a second infant, a boy, was born at term. He showed jaundice half an hour after birth. Four hours later jaundice was intense and the spleen and liver were enlarged. Two transfusions with blood from the father were given in the course of 24 hours. The infant died when 48 hours old. Necropsy showed characteristic extramedullary hematopoiesis as well as selective jaundice of basal ganglia of the brain (kernicterus). On the first day of life a red cell count was 1,980,000 and hemoglobin, 43 per cent, and on the second day these were 2,050,000 and 43 per cent, respectively.

Blood grouping of the family was:

	Group	*Rh*
Father	O	+
Mother	A	-
First child (male)	A	+
Second child (male)	O	+

The serum of the mother contained anti-Rh agglutinins to a titer of 1:8. The titer against B cells was 1:32.

CASE 3.—(Ju.) The mother had five healthy children. The neonatal histories of the first two make no mention of jaundice. The third developed jaundice on the third day of life. It lasted four days. The fourth child had intense icterus which appeared on the third day. The blood showed normoblasts. The red cell count dropped to 2,700,000 after two weeks. No transfusion was given. Recovery took place slowly. The liver, which was enlarged, eventually returned to normal size. The fifth baby, male, developed deep jaundice the day after birth. This increased until the third day and cleared up after seven days. The red cell count dropped to 2,500,000 and hemoglobin, to 50 per cent on the seventh day. A transfusion was given. The next day the red cell count had risen to 3,800,000 and hemoglobin, to 75 per cent. As was later ascertained, the donor used was fortunately Rh-negative. Stained films of blood did not reveal any erythroblasts. One and a half years later the child was normal. At this time blood grouping of the whole family was performed.

	Group	*Rh*
Father	B	+
Mother	A	-
First child (female)	B	+
Second child (male)	A	-
Third child (female)	A	+
Fourth child (female)	A	+
Fifth child (female)	O	+

The serum of the mother showed anti-Rh agglutinins to a titer of 1:64 still present one and a half years after the last delivery. The titer of β agglutinins was 1:256.

CASE 4.—(Ol.) A first baby, male, was born spontaneously at term. Eight hours after birth, pronounced jaundice was observed. At the

same time, cyanosis appeared and breathing became labored. The jaundice increased steadily. The spleen became palpable. The infant died after 48 hours despite a transfusion of thrice washed red cells suspended in normal saline. The cells were obtained from the mother's Rh-negative blood. Examination of the infant's blood showed 2,100,000 red cells, 60 per cent hemoglobin, 129,000 white cells (including normoblasts). Numerous normoblasts were seen in stained smears. Blood grouping of the family was:

	Group	*Rh*
Mother	O	−
Child (male)	A	+
Father could not be typed as he is overseas.		

The mother's serum contained anti-Rh agglutinins to a titer of 1:4. The titer for α agglutinins was 1:8, for β agglutinins, 1:256. Two months later only traces of anti-Rh agglutinins could be found. Serum from cord blood was also tested for the presence of anti-Rh agglutinins. Tests with known red cells were set up in the usual manner. No agglutination could be seen either with a magnifying lens or under the microscope. A large drop of the mixture was placed on a glass slide and reincubated for two hours. By this method, weak agglutination could be seen with all the Rh-positive cells whereas the Rh-negative cells did not show any clumping. This effect could not be produced by using only the slide method.

The history of the mother revealed that she had received seven transfusions during one month in the course of a general septicemia four and a half years previously. It was impossible to test the donors for their Rh constitution, but it seems reasonable to assume that most if not all were Rh-positive. No severe reactions following the transfusions are reported, but it is stated that after the last three, a slight chill took place and after the fifth transfusion, the urine became dark red in color.

CASE 5.—(Be.) The first two children born to this mother in 1928 and 1932, respectively, were normal at birth and are now well. The third pregnancy, in 1938, terminated normally with a living male child. Thirty hours after birth, pronounced jaundice was noted. This persisted until death. The red cell count was 4,400,000 and hemoglobin 76 per cent on the third day and these dropped to 1,350,000 and 41 per cent respectively, on the twentieth day, just before death, despite six transfusions, which at that time were given without regard to the Rh-factor. Fever was present on the fourth and fifth days and during the last week of life. Necropsy revealed generalized jaundice. The liver and spleen were enlarged. There were multiple small abscesses in the lungs and liver. No extramedullary hematopoiesis was seen. A fourth pregnancy in 1939 terminated in a breech extraction of a macerated fetus of approximately 7½ months' gestation. Pathologic examination, which was done a few days later, showed extensive autolysis. The fifth pregnancy, contrary to expectation, went to full term ending in the delivery of an apparently normal male infant. Two days after birth jaundice was noticed. This increased for some days and disappeared by the thirteenth day of life. The red cell count dropped from 5,300,000 on the first day to below 2,000,000 on the fifth day. It increased after two transfusions with washed Rh-negative cells, but fell again to 1,600,000 on the thirteenth day.

Another similar transfusion was given after which the red cells increased to 2,100,000. From then on the red cell count gradually improved. Four to six nucleated red cells were seen on the second day; subsequent films of blood showed 0 to 3. When seen two months later, the infant was almost normal. Blood grouping of the whole family gave the following picture.

	Group	*Rh*
Father	O	+
Mother	O	-
First child (female)	O	+
Second child (male)	O	+
Third child (male)	O	+

The mother's serum contained anti-Rh agglutinins to a titer of 1:32. The titer for α agglutinins was 1:64 and for β agglutinins, 1:16. Cord blood tested as described previously did not reveal any anti-Rh antibodies.

CASE 6.—(Fa.) The first pregnancy in 1936 terminated with the birth of a normal male infant. A second pregnancy in 1943, ended with the delivery of a male baby. Routine testing of mother's and infant's blood during the course of studies proceeding in this hospital revealed that the mother belonged to group AB, Rh-negative, and the infant to group AB, Rh-positive. An immediate test for anti-Rh agglutinins in the serum of the mother gave a strongly positive result, the titer being 1:1,000. At this time, no clinical signs of HAN were observed. A few hours later, jaundice became obvious. A red cell count was 5,025,000 and hemoglobin, 106 per cent. No erythroblasts were seen in stained blood smears. The next day the red cell count had dropped to 3,900,000 and hemoglobin to 92 per cent. A transfusion of washed cells obtained from the mother's blood was given that day and another the following day. Thereafter a red cell count of around 4,800,000 and a hemoglobin level of around 100 per cent were maintained until the eighth day of life, when the jaundice had cleared up. A further drop in the red cell count to 3,416,000 and hemoglobin to 84 per cent by the eleventh day was an indication for another transfusion. Rh-negative whole blood was used. The next day a red cell count was 4,920,000 and hemoglobin 109 per cent, but at the same time jaundice reappeared and remained for two days. When discharged from the hospital, the infant was pale but no jaundice was evident. The red cell count was 4,000,000 and hemoglobin, 83 per cent. Anti-Rh agglutinins of a low titer were found in the breast milk but not in the saliva or urine of the mother, or in cord blood. Blood grouping of the family was as follows:

	Group	*Rh*
Father	B	+
Mother	AB	-
First child (male)	B	+
Second child (male)	AB	+

Comment

These observations on six families represent many features of HAN. Common to all cases that could be tested (only one father was not available) was the combination of an Rh-negative mother, an Rh-positive father, and child. All the mothers had anti-Rh agglutinins in their sera to a higher or lesser degree.

The sex distribution of six known cases was four males, 2 females. If seven presumptive cases are added to these making a total of 13, ten were male and three female. Although this would appear to indicate a predilection of the male sex, the small numbers do not warrant any definite conclusion. Potter[6] reported 23 males and 13 females in 36 autopsies of infants who died of HAN.

Case 1 presents a typical history of HAN with increasing damage in successive pregnancies. The high titer of 1:1,024 for α agglutinins in the mother's serum is noteworthy. Apparently there was immunization not only by the Rh factor, but also by the normal iso-agglutinogens.

Case 2 demonstrates the ineffectiveness and possibly an injurious effect of transfusion with Rh-positive blood.

Case 3 shows that even after repeated immunization by 3 previous pregnancies with Rh-positive children, it does not necessarily follow that a severe form of HAN will ensue. In spite of the fact that agglutinins were demonstrable one and a half years after the last delivery, suggesting that the antibodies at the time of the pregnancy must have been of high titer, the infant made a satisfactory recovery.

Case 4 reveals the harmful effect of transfusions with Rh-positive blood to an Rh-negative woman. Although the transfusions (7 in the course of 4 weeks) did not cause any dangerous reactions in the patient herself (possibly the time interval between the first and last transfusions was too short), they were sufficient to immunize her to such a degree that her first child died of HAN 36 hours after birth in spite of a transfusion with Rh-negative blood. That immunization of the mother by transfusions rather than by the fetus was responsible for the severity of the disease in this case is supported by the fact that the iso-agglutinin titer for α agglutinins was only 1:8, and for β agglutinins 1:126. The child belonged to group A. This is in sharp contrast to case 1. Apparently very little if any A antigen passed through the placenta and the same is suggested for the Rh factor. It seems unlikely that only one of two antigens present should have passed into the maternal blood stream. That the A and B agglutinogens are able to immunize is shown by the rise of the corresponding agglutinins after transfusion with incompatible blood.

Two similar cases have been reported by Diamond[7] in one of which the offspring was afflicted with HAN even though the mother had previously received only one transfusion. It is therefore highly desirable that no female of Rh-negative constitution should be transfused with Rh-positive blood. Otherwise, her potential offspring may be endangered and possibly her chance of having a living child destroyed. Taking such precaution would of course also prevent the possible occurrence of a reaction due to anti-Rh agglutinins if she should subsequently happen to be transfused with Rh-positive blood.

Case 5 illustrates a well-known course of events in the first four pregnancies, i.e., a gradual increase in the severity of HAN. However, it is

interesting that the fifth pregnancy ended with a full-term living infant. The high titer of anti-Rh agglutinins, 1:64, found in the mother's serum is evidence that a considerable amount of antibodies had been produced by her.

In Case 6 the interesting features are the exceptionally high titer of anti-Rh agglutinins, 1:1,000 in the mother, and the fact that after the third transfusion with compatible Rh-negative blood (which was tested with a standard anti-Rh serum as well as with the mother's serum), jaundice reappeared in the infant. This suggests the possibility of a sudden massive destruction of red cells. This occurrence may possibly be explained by the use of fresh whole blood containing complement. The possible role of complement in the clinical picture of HAN will be considered later.

Discussion

The evidence so far accumulated supports the theory that HAN is brought about by the following sequence of events. As a result of the passage of Rh-positive blood from the fetus through the placenta into the maternal blood stream, anti-Rh antibodies are produced in her. These maternal antibodies are then transmitted through the placenta in the opposite direction from her to the fetus and hemolyze fetal red cells. Ninety per cent of cases fit into this explanation, and in the remaining ten per cent, it is assumed that other similarly acting antigen contained in the fetal red cells is responsible for the condition. It is interesting to speculate as to the mechanism which allows fetal Rh-positive red cells to immunize the mother whose blood is Rh-negative. It does not seem probable that whole red cells of the fetus would penetrate the placental barrier and enter the maternal circulation unless some pathologic condition permits of their passage. In this connection Javert[8] has reported the presence of hematomas in the intervillous spaces of 8 placentas out of 35 in cases of HAN. This is a rather low incidence, and furthermore, no control studies are mentioned as to the presence or absence of such lesions in instances in which the combination of an Rh-negative mother and an Rh-positive infant occurs without accompanying HAN. In the absence of some placental lesion, the red cell is probably too large to pass through the meshwork of reticulum but soluble proteins, antigenic in nature, might do so. It is possible that these soluble proteins contain the Rh antigen. A similar situation pertains to subcutaneous injections of bacterial vaccine. Following injection the organisms are not found in the blood stream, yet antibodies are produced against them. It seems likely that soluble antigenic protein molecules of very small size might find their way through the reticulo-endothelial system into the blood stream, and so stimulate the production of antibodies. The fact that only 2 to 4 per cent of Rh-negative mothers give birth to infants who present evidence of HAN, lends credence to the view that the Rh-factor may be of very small dimensions, and might therefore be a

weak antigen when administered intravenously.[9] Mothers may also vary in their ability to be immunized by the Rh-factor. However, a massive dose of antigen as a result of transfusion does immunize a resistant mother. Thus, Diamond[7] has reported an interesting observation of an Rh-negative woman who had four healthy children who were all later proved to be Rh-positive. She received a transfusion of blood from her husband who was Rh-positive with no apparent untoward effect. A child born following this had typical HAN, suggesting that immunization took place as a result of the transfusion rather than the preceding pregnancies.

Another point worthy of consideration is the variation in the clinical picture of HAN. It is reasonable to suppose that the amount of hemolysins produced and the amount transmitted to the fetus and the time when such transmission occurs will have an important bearing on the clinical manifestations of the disease. If hemolysis begins early in fetal life, miscarriage, premature birth, or stillbirth may occur; whereas, if a considerable amount of hemolysins is acquired later, i.e., toward the end of pregnancy, an apparently healthy infant may be born at full term and signs of HAN may not become evident until some time after birth. Indeed, a red cell count and hemoglobin determination just after delivery may show the presence of a slight anemia. This is usually overlooked since such examination is rarely done at this time.

It is a common observation that hemolysis may set in and progress after the cord is cut, and any further transmission of hemolysins is impossible. It has been suggested that the hemolysins are stored in the fetal tissues and so rendered innocuous for the time being, and that for some unknown reason, they are released after birth.[5, 10] Wiener and Wexler[11] imply that only when these storage places are filled to capacity during fetal life will the disease start in utero. According to Kariher,[12] the end products of red cell destruction are eliminated from the fetus in utero by means of an interchange of substances through the placenta, whereas after birth, they are accumulated in the infant. This could explain why jaundice may appear some time after birth, but not why some infants show severe jaundice at birth, and why the destruction of red cells may make such rapid progress in the first days of life and sometimes continue for weeks.

Hemolytic reactions as a result of α and β hemolysins as well as anti-Rh hemolysins are usually observed shortly after transfusion. It is difficult to understand why anti-Rh hemolysins should show a completely different behaviour in the fetus. The theory that they are stored away in the tissues, or in the reticulo-endothelial cells has been offered by Wiener and Wexler.[11] A different hypothesis may be proposed as an explanation. It is known that the amount of complement varies not only as between different persons, but also in the same person at different times. It is not known how much complement exists in the fetus, whether it is transmitted from the mother similar to antibodies, or when the fetus

begins to form it. It has been determined that the amount of complement in cord blood[13] and in the first days of life[14, 15] is distinctly smaller than the quantity found a short time later. There is also a wide variation between different cord sera. This comparatively small amount of complement in early life could explain the relatively slow action of the hemolysins in HAN as compared with their quick action in reactions following transfusion. Complement may have played a role in Case 6 where a recurrence of jaundice was observed after fresh Rh-negative whole blood was transfused.

Lack of complement would account for the fact that hemolysis may increase relatively slowly after birth, but it does not explain the fact that it may extend over a period of weeks. An explanation of this occurrence may be offered by some experiments of Pfeiffer and Friedberger,[16] and Bail and Tsuda[17] who noted that vibriolysins are not completely utilized by the process of vibriolysis in the peritoneal cavity of the guinea pig, but are set free after the destruction of the vibrios and can exert their action again. The authors concluded that no consumption of vibriolysins could be demonstrated by the process of lysis. These experiments differ from those of Bordet.[18] Pfeiffer[19] explained this difference by pointing out that Bordet performed his experiments with hemolysins in the test tube where no complete destruction of the red cell occurs, but only a bursting of the membrane, liberating cell contents, and that the stroma retains bound antibodies. However, in the living animal complete destruction of vibrio takes place. It is possible that the same may happen in the case of hemolysis occurring in a living body. If this could be shown to be so, it could explain persistence of the hemolytic process in the baby until the hemolysins, like any other passively introduced antibodies, are eliminated from the body. Since the serum containing the antibodies is of homologous character, it might tend to lengthen the period of elimination. Schütze[20] found that vibriolysins were present in passively immunized guinea pigs after 24 days, if homologous serum was injected whereas, if heterologous serum was used, they were present for only 6 or 7 days.

Until a few years ago, the diagnosis of HAN was made purely on clinical and hematological grounds. As a result of Levine's discovery, it is possible to anticipate its occurrence and thus make an early diagnosis, in some instances before clinical signs become evident. Determination of the Rh constitution of an expectant mother may be done at the same time as a sample of blood is drawn for a Wassermann or similar test. If she is Rh-negative, a test of the husband's blood will reveal the possibility of immunization by Rh antigen. If he is Rh-positive, his wife's serum may be tested shortly before the calculated time of delivery for the presence of anti-Rh agglutinins using the husband's red cells preferably for this test. If this blood cannot be used due to group incompatibility, any compatible Rh-positive cells may be employed. If the presence of anti-Rh agglutinins is demonstrated HAN may be suspected. Furthermore,

in all instances in which the mother is known to be Rh-negative, the presence or absence of Rh factor in her newborn infant should be determined immediately after birth. This can be done quite easily by using a sample of cord blood. If it is Rh-positive, the baby should be watched closely and have repeated hematologic examinations so as not to miss the first signs of the disease.

As reported by other observers,[11, 21] there was no correlation between the titer of anti-Rh agglutinins in the mother's serum at the time of delivery and the severity of the disease in her newborn infant. A very severe case was associated with a low maternal anti-Rh agglutinin titer and a mild or moderate one, with a very high titer. To account for this Wiener and Wexler[11] offer, the theory previously mentioned of storage of anti-Rh antibodies in the tissues, it might be explained in the following manner:

1. Only a fraction of the antibodies normally present in the mother's blood passes through the placenta into the fetal circulation. The size of this fraction varies and seems to depend upon the permeability of the placenta. Titrations of mother's and corresponding cord sera for iso- as well as hetero-agglutinins were performed. These showed that the percentage of transmitted antibodies varies considerably. Two of the most striking examples are given in Tables I and II.

TABLE I. TITRATION OF HETERO-AGGLUTININS (SHEEP CELLS)

SERUM OF		DILUTION OF SERUM									
		UNDILUTED	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512
No. 45	Mother	4+	4+	4+	3+	2+	1+	–	–	–	–
	Baby	4+	4+	4+	2+	±	–	–	–	–	–
No. 63	Mother	4+	4+	4+	4+	4+	3+	2+	1+	–	–
	Baby	1+	–	–	–	–	–	–	–	–	–

TABLE II. TITRATION OF ISO-AGGLUTININS (BETA)

SERUM OF		DILUTION OF SERUM									
		UNDILUTED	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512
No. 6	Mother	4+	4+	4+	4+	4+	4+	4+	3+	2+	±
	Baby	1+	±	–	–	–	–	–	–	–	–
No. 76	Mother	4+	4+	4+	4+	3+	1+	±	–	–	–
	Baby	4+	4+	2+	1+	–	–	–	–	–	–

2. The second and probably more important consideration is that we measure agglutinins in the test tube, whereas the determining factor in the body is the hemolysin. The power to agglutinate in vitro does not always correspond with the power to hemolyse in vivo. The same discrepancy between agglutinating and lytic effect exists in other sera. Anticholera rabbit serum, made with a single injection of $\frac{1}{10}$ loop of vibrios, usually has a high vibriolytic effect in the peritoneal cavity of guinea pigs, and often a low agglutination titer in the test tube.

The treatment of choice for HAN is early transfusion with a concentrated suspension of Rh-negative red cells. If the mother's serum contains anti-Rh agglutinins, it would seem desirable not to delay transfusion until the red cell count and hemoglobin drop much below normal. The number of transfusions will depend upon the course of the disease. In many cases two or three will be sufficient to carry the baby over the critical time. It is now generally agreed that only Rh-negative blood should be used since Rh-positive cells will undergo the same destruction as the cells of the infant and the resulting increase in bilirubinemia will place a further load on an already overburdened liver. Whole blood of even an Rh-negative donor should not be given if that person has ever received a transfusion of Rh-positive blood, or, in the case of a woman, given birth to an Rh-positive child. To test for the presence of anti-Rh agglutinins in such prospective donors' sera is not sufficient as hemolysins may be present which are not detected by the agglutination test. If such donors have to be used, their red cells should be washed and suspended in saline, or inactivated plasma of the same blood group. Treated in this manner, even the red cells of the mother herself can be given without danger. In the rare cases of HAN, where mother and newborn are both Rh-positive or both Rh-negative, washed red cells of the mother are the only ones which can be transfused safely, as it might be difficult, or impossible to determine the specific antibodies at fault, and to select suitable donors. Transfusions of washed red cells have been used in the treatment of HAN by Wiener and Wexler,[11] Brown and Levine,[10] and others. Levine[22] states it is probably not necessary to wash the mother's Rh-negative blood for the complete removal of her plasma. Red blood cells can be concentrated to the desired level, and possible transfer of antibodies and complement, which may be present and may prove to be harmful, is excluded. Transfusions of concentrated suspensions of red cells are recommended by Watson[23] and others, who found it to be satisfactory when the aim is to increase the oxygen-carrying capacity of the circulating blood. It is especially valuable when it is desired to obtain the maximum rise in hemoglobin with the injection of a minimum of volume.

Summary

In six families there occurred six cases of hemolytic anemia of the newborn, and there was evidence that seven other infants had probably suffered from this disease.

Common to all cases tested was the combination of the following conditions: The mother was Rh-negative, the father was Rh-positive (only one father was not available for testing), and the infant was Rh-positive. All the mothers had anti-Rh agglutinins in their sera.

Immunization of an Rh-negative woman by repeated transfusions of presumably Rh-positive blood was later followed by fatal hemolytic anemia of her first newborn infant. Rh-negative females should not be

transfused with Rh-positive blood to prevent the possibility of this undesirable effect upon any future Rh-positive offspring.

A possible role of complement and of the liberation of hemolysins after the destruction of red blood cells in the clinical picture of HAN is discussed.

No correlation was found between the titer of anti-Rh agglutinins in the mother's serum at parturition, and the severity of the disease in her newborn infant.

As the treatment of choice for this disease, the infant should receive a transfusion of a concentrated suspension of washed Rh-negative red blood cells as early as possible, and this should be repeated as often as may be necessary. A suspension of washed cells from the mother's blood may be used if no suitable donor is available. Washed cells from the mother's blood should be used in any case where the mother and her newborn infant who shows evidence of the disease are both Rh-positive or both Rh-negative.

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PSYCHODYNAMIC AND THERAPEUTIC ASPECTS OF FUNCTIONAL DYSMENORRHEA

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IN VIEW of the tremendous strain on feminine emotions, and the ensuing psychic stress caused by the impact of the war in general, the subject of dysmenorrhea is becoming one of growing importance. It is to be assumed that this complaint occurs not only as a result of certain irregular anatomic and pathologic conditions, but may appear in consequence of some psychic disturbance. Needless to say, the psychologic equilibrium of a woman may be adversely affected by other than war emergencies, and neurotic manifestations may well be the result of other disturbing experiences in her life.

Possible Neurotic Origin of Dysmenorrhea

It is the purpose of this article to point out the close relationship between dysmenorrhea and neurosis. A neurosis may be the sole or predominant cause of dysmenorrhea, or it may mold the signs and symptoms associated with gynecologic features exclusively.

There is a consensus of opinion that menstruation, as a physiologic phenomenon, should be free of any organic or mental discomfort; causes of the menstrual suffering are open to discussion. In the last few years, there is increasing evidence that any consistent anatomic lesion is absent (Julius Bauer,[2] Randall and Odell[8]). Psychic factors as the pathogenic principle are surmised by a growing number of authorities. Fairbairn[4] confirms this claim by discussing the results of cervix dilatation, Kurzrok,[11] after having meticulously evaluated the endocrinologic assets, is in favor of some psychic mechanisms. Similar conclusions were drawn by Emil Novak[7] and Leon Israel.[5] Space does not permit a complete list of all researchers whose work finally led to the same conclusion.

The psychotherapist feels that these testimonies do not substantiate the psychogenesis. He is in a position to furnish a workable theory which explains some dynamics of functional dysmenorrhea together with its concomitants; he can further explain why the different remedies and operations have an influence on the patient, not on her genitals, but on her personality as a whole. By approaching this problem, he chooses the means of the psychomotor reflex.

Psychomotor Reflex

It is understood that emotions are psychic acts provoking bodily features; these features are specific for any given emotion, and their

purpose is to clear away the tension resulting from any emotion. The unity emotion and bodily reaction is spoken of as psychomotor reflex.

Any one of the numerous qualities characteristic for neurotics is likely either to disturb a "normal" psychomotor reflex, or establish a new one under conditions alien to the normal being. Neurotics show vivid associations, they connect certain facts with experiences and vice versa. Therefore, menstruation is being connected with certain old events, experiences, queer ideas. Emotions, primarily belonging to this old material, are attributed to menstruation. In her dysmenorrhea, a woman is reminded of some situation of her past and, at the same time, is prevented from realizing this situation. This explanation is based on the concept of the unconscious which makes simple, logical explanation of this dependence ineffective to the sufferer. For that reason, a neurotic is never capable of correcting her misconceptions by experience.

The origin of dysmenorrhea is the (neurotic) belief that menstruation, a phenomenon of so great an importance and impact must afflict the sphere of feeling. Anxieties and fears are experienced, because some repressed material is touched upon; the neurotic associates anxiety with menstruation, thus establishing the vicious circle.

History

This assumption is corroborated by a dysmenorrheic girl's history. The most bewildering reports of her first menstruation can be obtained. She was caught by surprise, had no idea about its purpose, and reacted with fear of death. Opportunities to observe her older sister's menstruation were not utilized or, if experienced, completely forgotten under the impact of this frightening event. It is further astonishing how this girl's mother allegedly reacted to her daughter's first menstruation. She did just the contrary of what would be expected to appease the youngster's fears. It is obvious that tales like these are true only in exceptional cases; the psychologist must base his investigations on these fantasies, he must take them for granted. The truth will be found out later.

Another frequently reported reaction is the conviction that the patient has been wounded or mutilated. The bleeding is expected to be fatal. According to her temperament, a girl may respond with hyperactivity or lethargy. To boyish girls, the first menstruation means inevitable and mortifying womanhood, a fate against which they have been struggling all their lives. Finally, some girl was put into bed by her overanxious mother, thus pervading her with apprehensions.

Closer investigation shows the reasons for this behavior. It is the strict consequence of older experiences, either real events (trauma), or any condition which afflicted a girl adversely. That a parent's death

may act as a trauma, is undoubted. The same holds true for sexual experiences. One needs not think of some violent and terrible sexual scene; a mere trifle may act as strongly and lastingly as any real trauma. Arguments or dissensions in the parent's home, unhappy marriage, drunkenness or infidelity of a parent may call forth either protestation against her female role, or abhorrence of menstruation. These facts have shaped the conviction that menstruation and sickness are identical.

Clinical Symptoms

Dysmenorrhea is an organ neurosis, i.e., it is referred to suppressed material and shows the following characteristics of functional disease:

A. *Absence of an Underlying Pathological Anatomical Process.*—Since we were able to correct the conception "Nulla dysmenorrhea nisi obstructiva," no other organic cause was generally accepted as being present. This fact is supported by:

B. *Inconstancy of Pain.*—The degree of pain varies from month to month in the same individual, mostly as a reaction to pleasant or to distressing events.

C. *Reversibility.*—This is the outstanding characteristic of any neurotic symptoms. The entire process may be reversed, the body recovering its original normal function, no trace being left to show that a pathologic condition had ever been manifested.

D. *Connection With Other Neurotic Symptoms.*—(1) When a psychologic cure has been effected in a neurotic woman, menstrual cramps disappear, even when no treatment has been administered for the latter. This was first stated by Allers.[1] (2) In concentrated psychotherapy, multiple connections were found between dysmenorrhea and almost every neurotic symptom of the patient, a point more fully referred to later.

E. *Amenability to Various Medical Measures.*—In addition to the pronouncements of various authorities, it may be stated that at one time or another, a variety of drugs have been successfully employed in the treatment of dysmenorrhea.

F. *Suggestion and Hypnosis.*—This important curative process has been described by many investigators. Hypnosis, the most effective form of suggestion, has been found to bring about a complete cessation of dysmenorrheic cramps in a great many cases. Its employment, however, because of the attendant dangers inherent in the hypnotic procedure, is not recommended.

Sequelae

The neurotic element alters the symptomatology, complicates the disease, and renders it more difficult of diagnosis and cure. On the

other hand, there are cases in which the neurosis effects the disappearance of the dysmenorrheic syndrome, in which the following aspects can be observed.

1. *Development of the Complete Picture.*—Cramps are in the foreground, the menstrual lochia may be changed (duration, quality, and amount), premenstrual discomfort can be observed and other neurotic symptoms harass the patient.

2. *Stationary.*—There is little to say about those women who tolerate discomfort and attribute their pains to womanhood. In the words of a novelist, they regard themselves as the "Slaves of the Moon."

3. *Changeable.*—The amount of pain varies during each period, and the patient can give no reason for this change. A scrutiny of the history, however, reveals the fact that the degree of pain varies regularly with some pleasant or unpleasant experience. For example, a word of praise from her employer may cause the pain to diminish, while excitement precipitated by discord between the patient and her husband or mother may bring about an increase in the severity of the pain.

4. *Disappearance of Dysmenorrhea.*—In the majority of cases this occurs either through the influence of sexual activity, pregnancy, etc., or through fortuitous circumstances of minor importance. Cases of spontaneous (untreated) disappearance deserve the fullest attention, because in these, while the symptom is removed, the underlying cause persists and is apt to produce some other symptom, either organic or neurotic in character. It remains to be demonstrated whether there is a relation between the "cured" dysmenorrhea and the symptom which follows the cure. In such cases the appearance of diarrhea, constipation, gastric discomfort, heart palpitations, migraine, etc., can be observed. The development of certain compulsions is also quite frequent, especially an exaggerated desire for self-cleansing. Depression is another quite common substitute, or a slight loss of sexual feeling, when freed from cramps.

5. *Recurrence of Dysmenorrhea.*—As is well known, dysmenorrheic cramps sometimes reappear after a period of cessation. Frequently, this fact is overlooked if it occurred prior to gynecologic examination, yet a knowledge of it is valuable in arriving at a clear understanding of the patient's history.

I had occasion to observe such a recurrence in a patient who, at the time of re-experiencing cramps, was not menstruating.[10] She was thirty-three years old, unhappily married, and the mother of three children. Her cramps had stopped after her first confinement. Her sexual feeling was unstable, she was able to experience full climax only by masturbating, but never during intercourse, for she had imagined, unconsciously, that there was something in her womb. When, in the course of treatment, this unknown something was determined by eliciting the traumatic situation, her cramps reappeared, without menstruation.

It has been the experience of many investigators that complete cures can be effected more often and with greater ease among young patients than in cases where dysmenorrhea has been present for a long time. A variety of treatments have brought about cures, particularly when the treatment dealt with the causes basically responsible for the illness of the individual. Some physicians are excellent psychologists by nature, and are thus able to choose promptly the most appropriate procedure. Many other conditions may also be helpful in working toward an elimination of the symptom as, for instance, the patient's growing weariness with it, or else, the relation between the gynecologist and his patient (Freud's term, "transference"), or any occurrence which tends to wipe out the pathogenic neurotic idea underlying the dysmenorrhea. Psychologically speaking, this group presents monosymptomatic neuroses, an expression which is easily understood.

Definition of Dysmenorrhea and Its Concomitants

In accordance with the above concept, it is proposed to include in "functional dysmenorrhea" a symptom complex associated with menstruation which affects, in addition to the pelvic organs, the personality as a whole. It would appear that all features manifested by the dysmenorrheic patient seem to be suppressions and conversion symptoms. All symptoms are closely interrelated and each supports and perpetuates the other; thus constituting a vicious circle which can be broken on either the physical or psychological level.

Dysmenorrhea may manifest itself in three different spheres:

Local.—Cramps; duration and intensity of flow; quality of the lochia accompanied by a feeling of heaviness in the regions of the uterus, pelvis, groin, backbone, etc., disturbance of urination as frequency, retention or incontinence; and of the defecation, as constipation or diarrhea.

General.—Manifestations in other organs which show a temporary and casual connection with the menstruation, i.e., in the stomach (anorexia, change in appetite), all forms of headache, heart symptoms of a neurotic character, etc. The secondary sexual characteristics at different sites of the body may be involved both organically and psychologically (skin, mammary glands).

Psychosexual.—Mental fatigue, anxiety, compulsion-like features, hypochondriacal symptoms, aggressiveness, craving, etc., are indications of menstrual disturbances. The sexual desires and impulses often become modified to the extent of being completely reversed, thus generally affecting the libido as to its intensity, direction, and form of expression.

In the psychologic approach it is essential to make a distinction between primary and secondary dysmenorrhea, as the former offers more resistance to psychotherapy than does the latter. Primary dysmenor-

rhea begins with the menarche, while secondary dysmenorrhea appears after a number of normal painless menstruations.

This definition of dysmenorrhea should shed light upon a number of complex questions of great importance which puzzle the physician. As stated, there is little significance in the cessation of the menstrual cramps in the majority of cases. The underlying cause persists, while the form of its expression takes another aspect. This may result in a new symptom giving rise to disorders of varying intensity, which often crop up only after a certain lapse of time. An occurrence in a patient's life, causing strong emotion may call forth the new symptom, especially if the event holds symbolic meaning and has any relation to those repressions which provoked the original dysmenorrhea. A state of anxiety may follow an operation, an abortion, or confinement, although this does not always occur. Women passing through the menopause may also be similarly afflicted. The death of a child, or any frustration, may become the cause of a neurotic condition which, in turn, may progressively transform itself into a psychosomatic phenomenon. The following observation will serve to demonstrate these points.

Psychotherapeutic Cure

CASE 1.—A colored woman, single, and twenty-eight years of age suffered from menstrual disturbances which consisted of fainting spells, vomiting, urinary frequency and severe cramps which confined her in bed during the first two days of her menstrual periods. Following a nervous breakdown, six months before the first interview, she had been stricken by these symptoms during each period.

Her first menstruation, which occurred at the age of thirteen, had surprised and bewildered her, and finally impressed upon her the terrible fear that she would bleed to death. She tried to clear the blood away by washing her genitals. Her grandmother comforted her, and gave sanitary advice and enlightenment about the menstrual cycle. The subsequent menstruations were accompanied by some pain which, by the time she became eighteen, was rather distressing. As she spoke, the patient uttered concern as to her ability to become pregnant. She now volunteered the information that during her eleventh year, she had been terribly upset by the death of her mother during a delivery. Next she discussed her recent nervous breakdown which she alleged had increased her menstrual discomfort, and had driven away her lover who feared that she was going crazy.

This history warrants a thorough investigation of three events: the first menstruation, the severity of the menstrual pain in her eighteenth year, and the influences which brought about the nervous breakdown. It was not possible to undertake such a comprehensive psychotherapeutic task in the clinic. However, in support of the assumption that these three stages of her neurosis are fundamentally contained in her first menstruation, is the concern about childbearing.

For this reason, the investigation was designed to elicit only a few paramount features of the nervous breakdown. She stated that she had enjoyed sexual intercourse with her lover, but, because of fear of

pregnancy for which she felt she was too young and unprepared, she had restricted intimacy to once a month. This same fear caused her to reject her lover's marriage proposal and provided him with the idea that she was losing her sanity. She reacted with a depression when she realized that her romance had been broken up.

She opened the second session with the report that her last menstruation, though somewhat painful, had been free from vomiting and fainting spells. The patient was highly grateful for this slight improvement.

She described a pleasant dream in which she had walked in her grandmother's pasture and milked the cows. In her associations she referred to her mother's tragic death from childbirth. Her mother and father had constantly quarreled, often violently, and the patient, as a child, had been under much stress when she witnessed these outbursts. She was never able to make up her mind as to which parent she should defend. After her mother's death, she had the ever-present fear that she herself might succumb to the same cause. She saw in the dream a desire to lead a peaceful life, but she thought that the memory of her mother's death might be too much for her to overcome.

During her third visit to the clinic, she announced that her menstrual pain was considerably relieved, and that she had not had urinary frequency, or any of her other former symptoms. Her guilt feelings connected with her mother's death were brought to her consciousness, and this part of her neurosis was made less forceful.

The succeeding menstrual periods were free from any symptoms, except for the experiencing of a slight pain if, at this time, she was confronted with an unpleasant situation.

From this report it is clear that the patient was strongly antagonistic toward her mother. Menstruation brought unconscious memories of the death of her mother. Suppression of the identification with her mother had prevented her from a friendly and affirmative attitude toward her own womanhood, against which she protested during each menstrual period.

CASE 2.—With the onset of her menstrual period, a colored girl, nineteen, was stricken with intense cramps which sometimes remained with her until well into the second day. For at least the first three hours and sometimes for the entire first day, she had to stay in bed. She never ate during the first day because she was afraid of vomiting. In this case, as in Case 1, some urinary discomfort was present. The gynecologic examination was negative, but the patient was disfigured and showed remnants of severe rickets. She was a highly intelligent girl, observed sharply and clearly, and was capable of judging quickly and astutely.

She vividly described her first menstruation. "When I noticed the blood I was terribly excited because I'd never heard of such a thing. I believed I had an accident, had hurt myself, and the bleeding would never stop. If I urinated, the bleeding increased. I noticed that my dress was stained and I believed that I had sat down in some dye or, perhaps, I had swallowed some glass. Finally I confided in my mother who told me it will come every month. I was dreadfully scared."

The girl was profoundly resentful of the mother's attempts to dominate her life and the lives of her four sisters. She despised her mother for constantly reproaching the father, who, as the result of an accident,

was a helpless invalid. The girl wanted to leave this sad environment, but she was handicapped by her disfigurement.

She was shown how her hatred for her mother had influenced her attitude toward life. This hostility may have deprived her of the possibility of objectively considering plans for her own future. The strong emotion may have been turned against herself as happens frequently in such cases. For instance, in her determination to differentiate herself completely from her mother, she bitterly hated any resemblance she had to the parent. Such a protest, if connected with the menstruation, may call forth all of her menstrual difficulty.

When these thoughts were presented to the girl, she confirmed their correctness by revealing many additional anamnestic details to those she had already given. She stated that she had never been aware of the menstruation of her older sisters, and it was as though she had been in dread of knowing about this phase of a girl's life. On the other hand, she had been cognizant of her mother's menstruation, and this was another proof of her hostility toward the mother whose menstrual flow was, to the girl, another expression of the woman's abominableness.

In both cases presented, urinary frequency was manifested, and though in the second case it seemed less severe, it harassed the patient considerably and therefore needs some discussion. She was asked about her toilet-training. Until the eighth year, she had been a bed-wetter and for this reason, her mother had taken her to various physicians until one of them said that the enuresis was merely a mischievous deed. The mother then felt obliged to punish the little girl who consequently felt ashamed and disgraced in the eyes of her neighborhood playmates. When menstruation came, she was unconsciously reminded of her earlier lack of urinary control. (A similar psychology is descernible in the first case, the link being masturbation.)

In the menstruation which followed this revealing session, the patient was almost free from discomfort, had no pain, was active and ate normally, but in a mild degree her urinary distress remained. The next menstrual period, however, was entirely without disorder.

Unfortunately, patients who are subjected to psychotherapy at a clinic tend to be uncooperative when it comes to follow-up studies. Only a small number consults us if a relapse occurs. Almost invariably, they dislike to contact us if they have been cured. To many of them, psychotherapy is a magic procedure, especially if, after a few sessions, a symptom which has been with them for a long time, disappears. They are fearful unless further contact with the physician may jeopardize the achievement they have attained.

These two cases have shown a psychology which is typical of that encountered in a large proportion of dysmenorrheic girls. Greatest stress should be put on the first menstrual period, especially if the girl considered it a peril. The reactive panic contains some elements which can be elicited in other features of the same patient's neurosis. Menstruation becomes the realization of old guilt feelings, evidence that old apprehensions are becoming true and substantial. Most of these guilt feelings are directed toward the mother, against whom the adolescent girl may have exhibited aggressive, hostile, or unfriendly thoughts. Therefore, these conceptions are based on suppressed material. Enlightenment only penetrates the upper layer of the mind and can never

reach the depths where the repressions are harbored. For that reason instruction, as well as the patient's own experience remains almost ineffective. It is true that the reality of the following menstruation diminishes the fears experienced with the first one, but the guilt feelings are apt to create another outlet.

In the first patient, frigidity was present. The patient professed to enjoy intercourse, but practiced it only once a month. In her report the connection between her dysmenorrhea and frigidity is obvious and needs no further correlation. As her dream and the first association to it show, every pleasure is overshadowed by her thoughts about her mother's terrible fate. A similar connection can be seen in the history of another patient.

CASE 3.—A woman of twenty-five, with a history of two operations,[9] complained about typical hysterical symptoms, including dysmenorrhea and frigidity. About the latter she was extremely concerned. Her primary dysmenorrhea was rather mild, and was replaced by some discomfort in the scar after oophorectomy. At the same site, sensations akin to vaginismus were experienced during intercourse. For the three menstruations preceding psychotherapy, menstrual pain had reappeared, increasing in intensity with each successive period.

The insecurity of her first marriage was carried over into the second and had influenced her feeling for her second husband to whom she was deeply devoted. When she experienced her first orgasm after one year of married life, her dysmenorrhea reappeared.

A dream recalled a sexual trauma which had occurred at the age of six and after I told her the trauma was the cause of her hysterical symptoms, they ceased. On the other hand, she expressed a strong resistance to the primary probing, a common reaction in neurotics. Dysmenorrhea was one manifestation of her resistance. Though reassured that even a temporary increase in the intensity of cramps should not cause alarm, the patient, nevertheless, consulted her family physician who referred her to the hospital where a presacral sympathectomy was performed. Following the operation, the patient experienced more excruciating pains than before. She decided to return for a continuation of psychotherapy.

Further psychologic study found that both dysmenorrhea and frigidity had their origin in a trauma caused by a sexual assault upon the patient in her sixth year. In marriage, orgasms were repressed in order to shut out the memory of this occurrence and the very same mechanism was responsible for dysmenorrheic cramps.

The preceding report touches upon the rather typical connection often observed between dysmenorrhea and frigidity.

Some dysmenorrheic patients discuss their frigidity without false modesty, while others shy away from the subject. The relation between dysmenorrhea and other neurotic symptoms must be investigated and qualified, otherwise the diagnostic means are not exhausted.

A similar result of the sympathectomy, in the author's experience, is rather common in neurotic patients. Extirpation of a relatively small number of nerve fibers is unlikely to sever all connections between the

uterus and the central nervous system. The psychic effect of this operation is tremendous; therefore, a psychologic examination of patients whose dysmenorrhea was cured by sympathectomy may throw some light upon this mechanism.

Pathologic Menopause

The neurotic features of a dysmenorrhea shape the manifestations of the pathologic menopause. This period is influenced by almost every disease which an individual had during life, complicated by both endocrine and psychic characteristics. E. Bleuler[3] stresses the similarity between the symptoms of puberty and those of the menopause. If a patient's reaction to her first menstruation or to the appearance of the earliest signs of puberty is examined, it will be found that there is much in common between the two. This may explain the variety of climacteric disorders.

CASE 4.—The history of a white woman, married and forty years of age, seeking relief from menopausal symptoms, is complicated by attacks of asthma. Five months prior to consultation, the patient was subjected to x-ray castration for fibroids and hemorrhages. Asthma bronchiale was twice manifested, the first series of attacks occurred during the delivery of her first child and was cured by a visit to her native country. Ten years later, after her second pregnancy, her asthmatic attacks recurred. Medical care relieved her of this symptom for a time.

About one month after irradiation, these attacks reappeared again together with her first "hot flushes," dizziness, vomiting, and feeling of emptiness in the head which augmented her climacteric symptoms. Stilbestrol controlled these attacks, but its use seemed contraindicated by the patient's tendency to bleed. She had suffered from a tuberculous pleurisy combined with pneumothorax when she was sixteen. Attacks of asthma regularly followed dreams or quarrels with her husband and children.

The patient's description of her marriage portrayed an incessantly frustrated woman. She married at twenty-four, became pregnant immediately and showed much concern about her husband's devotion, of which she had felt insecure due to the change in her appearance because of pregnancy. When her asthma was manifested, her husband left no stone unturned to help her; he had consulted numerous physicians and had sent her to different spas. Finally, her native country relieved her from this symptom.

The patient's sexual feelings became moody. For some time she did not experience any orgasm, but for some unknown reason, it came back and was strong again. After the second confinement, fear of another pregnancy dominated her to the extent that she hardly consented to intercourse. After the x-ray castration, the patient became aware of a kind of defectiveness, and that sensation made her hypersensitive and so irritable that she had constant quarrels with her family.

She had suffered with severe menstrual symptoms from her menarche at the age of fifteen. At that time she was exposed to great hardships. Because her native country was at war, she had to move, was devoid of the slightest comfort of living. When she had noticed her first period,

she went through an ordeal of fears and apprehensions. She depicted a state of dyspnea which she had experienced at that time, and which she believed was due to menace of the war. Dreams showed the source of these dyspneic attacks. She was never enlightened about sexuality, and was never conscious of the difference between the sexes. At the age of twelve, a cretin exhibited his genitals to her, and the patient believed she was about to get the same organs. This occurred at a time when she was alarmed by the pubertal changes of her body. This experience was forgotten, but revived with her first menstruation. This apprehension was kept alive for a long time and regularly induced dyspneic attacks. After she had manifested the tuberculous symptoms, the character of her dyspnea was changed and the latter disappeared completely after cure of the pleural symptoms.

When the patient was first seen, she was conscious of the fact that asthma and climacteric manifestations substituted for each other. When she experienced flushes, the asthma subsided and vice versa.

During treatment, the patient brought forth another interesting dependency; she was able to alleviate her menopausal symptoms by an enema. This fact led to the investigation of her conceptions about pregnancy which the patient had never ceased to fear. The growth of her fibroid and the subsequent bleeding irregularities gave her much trouble, once in favor of pregnancy and on the other hand refuting it. All these emotions were transformed into a deep hatred of her husband who enjoyed relations with her despite her troubles. She became extremely hostile to him, but was ashamed of these feelings.

When these dependencies were elucidated, the patient's symptoms subsided. The noxious principles of her puberty seemed to lose their hold upon her; follow-up showed that she had acquired a well-integrated personality. For the last two years she did not experience a single attack of asthma, and her other symptoms, although present to a slight degree, did not concern the patient.

The individual features peculiar to each clinical picture will reveal the factors responsible for the symptom in question. The clinical picture of every woman passing through the climacteric depends on three components: (1) the patient's constitution; (2) the residuals of her former illnesses; and (3) the neurotic trends, one expression of which may be dysmenorrhea plus its transformations and variations. In every case it is incumbent upon the physician to determine how far and to what extent a neurosis may affect the climacteric features.

Suggestions for Treatment

Having described several concomitants and corollaries of functional dysmenorrhea, some suggestions may be appropriate concerning the management and treatment of this symptom in patients whose psychologic conflicts are of a superficial character. Some women feel that menstrual discomfort is dependent upon their frame of mind. Whether false or true, such a statement may be helpful in approaching the psychic cause in a particular case.

The preliminaries do not differ from any routine examination. The physician listens attentively to the patient's descriptions of her men-

strual ailment and even encourages her to bring out details. Every comparison made by the patient is significant; for example, should she associate cramps with confinement, this would be a cue to her strong preoccupation with this subject in one way or another. The statement, "I feel so irritable, I would like to jump out of my skin," may be a protest against womanhood. A childless woman, by this same statement, expresses her resentment of her sterility, while in another patient menstruation may remind her of a miscarriage which she had suffered, and she gives expression to her grief through such articulation.

By close collaboration with the patient, the physician discovers the meaning of such statements. It is never possible to apply the solution found in one patient to another. The same utterance used by different patients may have other meanings, may be related to different epochs of their lives, and directed against various persons. Nevertheless, the elucidation of one situation alone may sometimes alleviate or even cause the disappearance of the neurotic part of the symptom and, by this means, the symptom itself.

Patients suffering from secondary dysmenorrhea may be subjected to this treatment, since the reasons underlying the symptom are easily accessible. A case in point is that of a girl of nineteen who suffered from menstrual cramps and manifested dysmenorrhea six months after the onset. In the course of her examination it was revealed that, when menstruating, she had been ordered by her mother to perform a task necessitating her prolonged immersion in a cold brook. At that time, she experienced her first attack of cramps. All subsequent menstrual periods were accompanied by a burning sensation. As a result she remained in bed the first two days of her indisposition. When talking of her mother, she exhibited strong emotions of hate. She confessed that she was an illegitimate child and that this had made her life miserable. When shown in detail how her own feelings had influenced her and had prevented her from attaining contentment in life, the patient realized the explanation. The advent of favorable circumstances, being courted, and improved prospects as to employment, brought about a change in her neurotic attitude. These elements were used to adjust the patient to reality and help detach her from her neurotic dysmenorrhea, evidently a consequence of the fixed preoccupation with her unhappy past and the numerous disappointments of her childhood.

When dysmenorrhea is manifested only after an abortion, the abortion may be the cause. Regret and sorrow at the loss of the child, or a need for self-punishment, may produce this symptom. The same may be true of a frustrated love affair, or marital discord. Nongenital ailments may also produce this symptom.

Conclusions

It is impossible to describe all neurotic concomitants of dysmenorrhea in the close compass of this paper. This syndrome, like "every medical

problem, includes a psychologic component,'' M. D. Mayer.[6] It warrants earnest study and a most thorough examination. The consideration of one factor as the only etiologic principle remains fragmentary; the honest researcher is uneasy until he has considered all sides of this baffling question. The evaluation of the whole personality is achieved, if we regard both the organic and the psychic makeup of the patient.

The importance of the symptom diagnosed as dysmenorrhea has been underestimated even in the psychiatric literature. If we direct our attention to all its features, it is not as changeable as is generally assumed. To use a comparison, it behaves like an iceberg, whose bulk is submerged, leaving only a very small part of the mass visible. It must be stressed again that the majority of sufferers prefer to retain the symptom of pain, especially if it is not too severe. This apparently masochistic trait is one of the many peculiarities, common to many a neurotic feature, but intelligible to those who have some insight into the nature of neuroses.

In this paper only a partial description of the psychologic aspect is given, and many readers, therefore, may find their observations somewhat at variance with those described here. The protean exterior of the symptom, the underlying causes of which are not yet obvious, but hypothetical, presents itself differently to each investigator. The neurotic patient shows to each observer another facet of this polymorphic structure.

Summary

1. As a psychosomatic entity, dysmenorrhea is understandable, if the psychic mechanism can be explained by carefully elucidating the history. The psychogenesis is coordinated to the neurosis and all its symptoms.

2. A definition of this symptom is given in an effort to comprehend all its manifestations, and to relate them to the whole personality.

3. The persistence and manifestations of the underlying psychic energy are shown in two case reports; in another, the dysmenorrhea was replaced by other neurotic symptoms.

4. Psychotherapy in secondary dysmenorrhea seems promising, as demonstrated in one case report.

5. Another feature of this symptom is, in the author's opinion, the fact that its investigation provides an approach to the unconscious of neurotics in any psychotherapeutic procedure.

Acknowledgment must be made to Dr. Max Schneider who examined Cases 1, 2 and 4 and referred them for psychic treatment.

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1192 PARK AVENUE

FETAL ELECTROCARDIOGRAPHY AND STETHOGRAPHY

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THE following study consists of single observations upon 22 pregnant women in various stages of gravidity. An attempt to record a fetal electrocardiogram and stethogram was made on each subject. Three cases were discarded because of technical difficulties.

Graphic methods for the study of the fetal heart were attempted as early as 1906.[1, 2, 12] These attempts were intermittent and largely unsuccessful because of technical difficulties. It was not until after 1930[3-11] that improved technique resulted in the registration of clearly discernible fetal electrocardiographic deflections. With the recent introduction of various amplification devices an ever increasing percentage of positive fetal electrocardiograms has been obtained.

Since the degree of amplification of fetal electrical potential determines the successful registration of fetal deflections, a greater percentage of positive tracings has been obtained with a tube amplifying apparatus than with a string galvanometer. However, with the string loosened to double or triple standard (1 millivolt to 2 or 3 cm.), the string galvanometer will yield positive tracings in a considerable number of cases.[13-14] This was the method employed in our study.

Graphic registration of fetal heart sounds is a more recent development. Fetal heart sounds were recorded on phonographic discs as early as 1923.[25-29] The first recorded fetal stethograms were reported in 1938.[30] To date, there have been few published studies of fetal stethography.[31-41]

Technique

The patient was placed in the dorsal position. The limb leads were discarded early in our study because of the uniformly negative results. Abdominal leads were taken by placing the limb electrodes upon the following sites: right upper quadrant paired with symphysis (RUQ-S); epigastrium paired with symphysis (E-S); left upper quadrant paired with symphysis (LUQ-S); right umbilical region paired with left umbilical region (RUR-LUR); right lower quadrant paired with left lower quadrant (RLQ-LLQ). The right arm wire was attached to the first electrode, the left arm wire was attached to the second electrode and lead one was taken. The string was adjusted for a deflection of 2 to 3 cm. for one millivolt of current.

For stethography the following technique was employed. An attempt was made to locate the point of maximum intensity of the fetal heart with an ordinary stethoscope. If detected, the microphone was placed over that site and held in place by a rubber belt. In cases where no fetal heart sounds were audible, the microphone was placed in each of the four quadrants.

Material

The subjects used were picked at random from the ante-partum clinic of the Bronx Hospital. The gravidity of the patients varied from 5 months to just before term.

Electrocardiographic Findings

Of the 19 cases studied, nine showed easily discernible fetal deflections occurring at regular intervals. One case showed occasional irregularly spaced fetal deflections and 9 cases failed to record any deflections in any of the leads. Percentage of positive records is 53. In our study it would appear that fewer positive tracings are obtained in the seventh and eighth months than in fifth, sixth, and ninth months. Only 2 cases out of 8 in the seventh and eighth months were positive whereas 8 cases out of 10 showed fetal deflections in the fifth, sixth, and ninth months.

TABLE I. GRAVIDITY

Months gravid	5	6	7	8	9
Number of cases	3	3	3	5	4
Number of positive tracings	3	2	1	1	3

Inasmuch as previous studies not included in this analysis failed to reveal any fetal deflections under five months' gravidity, such cases were omitted from this study.

TABLE II. WEIGHT OF MOTHER

Weight (in pounds)	120 to 140	140 to 160	Over 160
Number of cases	8	7	4
Number of positive tracings	4	5	1

The age of the mother and her parity had no bearing on the incidence of positive fetal electrocardiograms. Similarly, the presentation of the fetus and its sex were not determining factors in the obtainment of positive tracings. The weight of the mother appeared as a factor in the incidence of positive tracings, the greatest number having been obtained in the weight group of 140 to 160. It is reasonable to suppose that the weight of the fetus at the time the record is taken (not its birth weight) is a factor.

TABLE III. LEADS SHOWING NUMBER WITH POSITIVE FETAL DEFLECTIONS

RUQ-S	E-S	LUQ-S	RUQ-LUQ	RUR-LUR	RLQ-LLQ
5	6	6	0	1	2

This demonstrates that the best leads were those connecting the fundus uteri to the symphysis pubis. We previously noted that the mothers' limb leads were uniformly unsuccessful and were therefore discarded.

TABLE IV. TYPES OF FETAL DEFLECTIONS

	SINGLE UPWARD DEFLECTIONS	SINGLE DOWNWARD DEFLECTIONS	DIPHASIC DEFLECTIONS
Number of Patients	1	6	3

It has been noted by other investigators that a downward fetal deflection is indicative of vertex presentation, and an upward deflection

denotes a breech presentation. All of our positive cases were delivered as vertex presentations. The one case of upward deflection in our series was taken at six months' gravidity. At that period of gestation the presentation is not fixed, and consequently, it may have been a breech which rotated spontaneously to vertex at term.

Amplitude.—The amplitude of the deflections ranged from ¼ mm. to 3 millimeter. It is interesting to note that the three cases with the largest deflections were diphasic.

Rate.—The fetal rates varied from 125 to 150. No relationship between the fetal rate and the sex of the fetus was noted in this study. The rhythm was regular in all but one. The latter showed sinus arrhythmia.

Fetal Stethography.—Of the 19 cases studied, successful fetal stethograms, with both heart sounds, were recorded in 13 instances; one sound

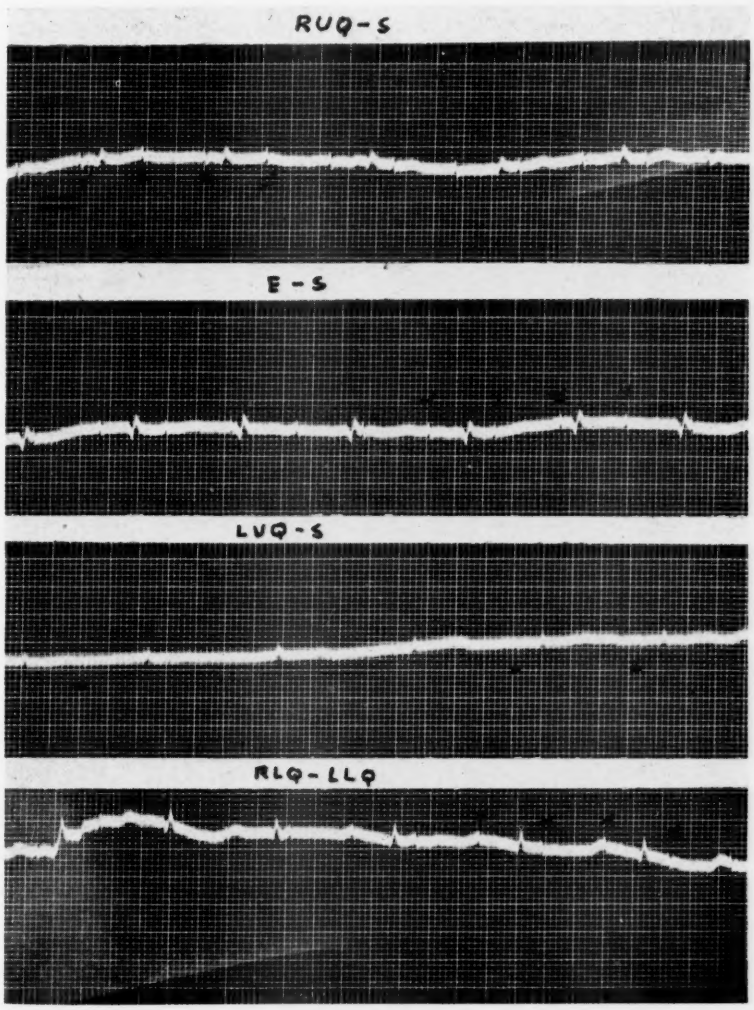

Fig. 1.—Case No. 10. Six months gravid. *A*, abdominal lead, right upper quadrant to symphysis; *B*, abdominal lead, epigastrium to symphysis; *C*, abdominal lead, left upper quadrant to symphysis; *D*, abdominal lead, right lower quadrant to left lower quadrant; *F*, fetal electrocardiographic deflections.

only in two cases. In four cases no stethograms were obtained. No attempt was made to measure the amplitude of the sound deflection because the latter could be varied at will by varying the magnification of the recording instrument. The number of deflections making up the first sound varied from 2 to 6; the number of deflections making up the second sound varied from 2 to 4. In most instances both first and second sounds were made up of 3 deflections. The duration of the first sound varied from 0.03 to 0.06 second. The duration of the second sound varied from 0.03 to 0.05 second. The first sound was longer than the second sound in 6 cases and equal to it in 6 cases. In only one instance was the second sound longer than the first.

Practically all of the first and second sounds assumed one of three patterns resembling M, N, or W.

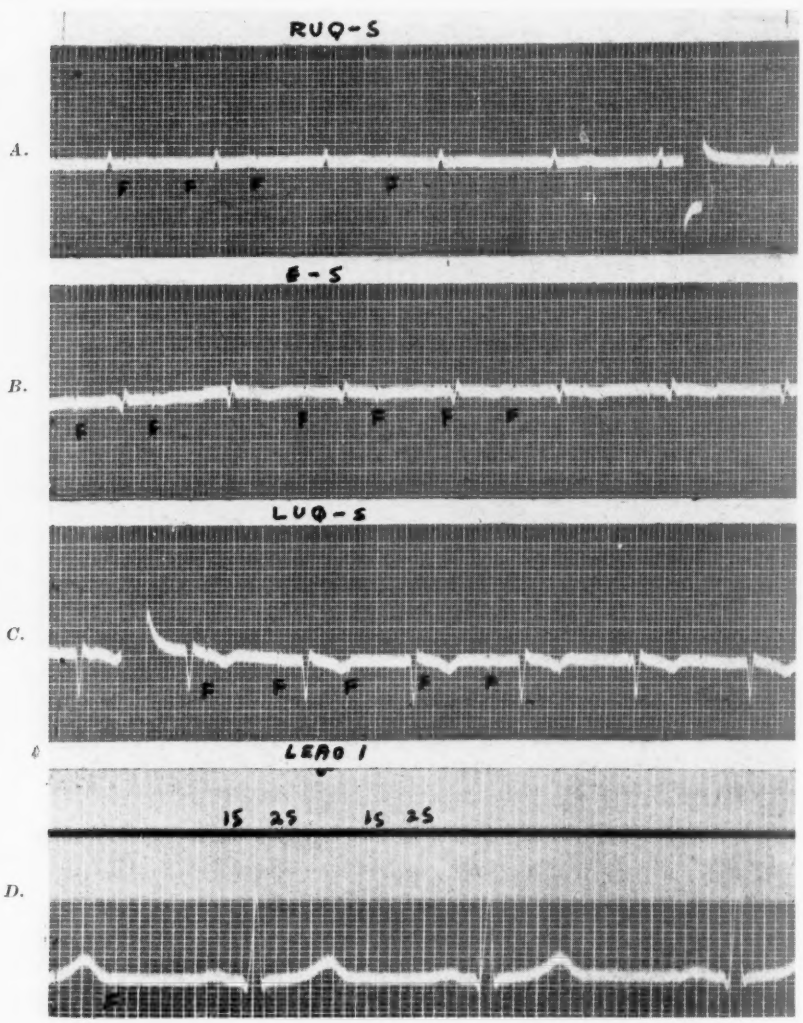

Fig. 2.—Case No. 23. Nine months gravid. *A*, Abdominal lead, right upper quadrant to symphysis; *B*, abdominal lead, epigastrium to symphysis; *C*, abdominal lead, left upper quadrant to symphysis; *D*, fetal stethogram, mother's electrocardiogram; *F*, fetal electrocardiographic deflection; *1S*, first fetal heart sound; *2S*, second fetal heart sound.

The duration of systole was shorter than diastole except in two cases in which they were equal. The duration, of course, depended upon the fetal heart rate and varied from 0.18 to 0.20 for systole and from 0.20 to 0.30 for diastole.

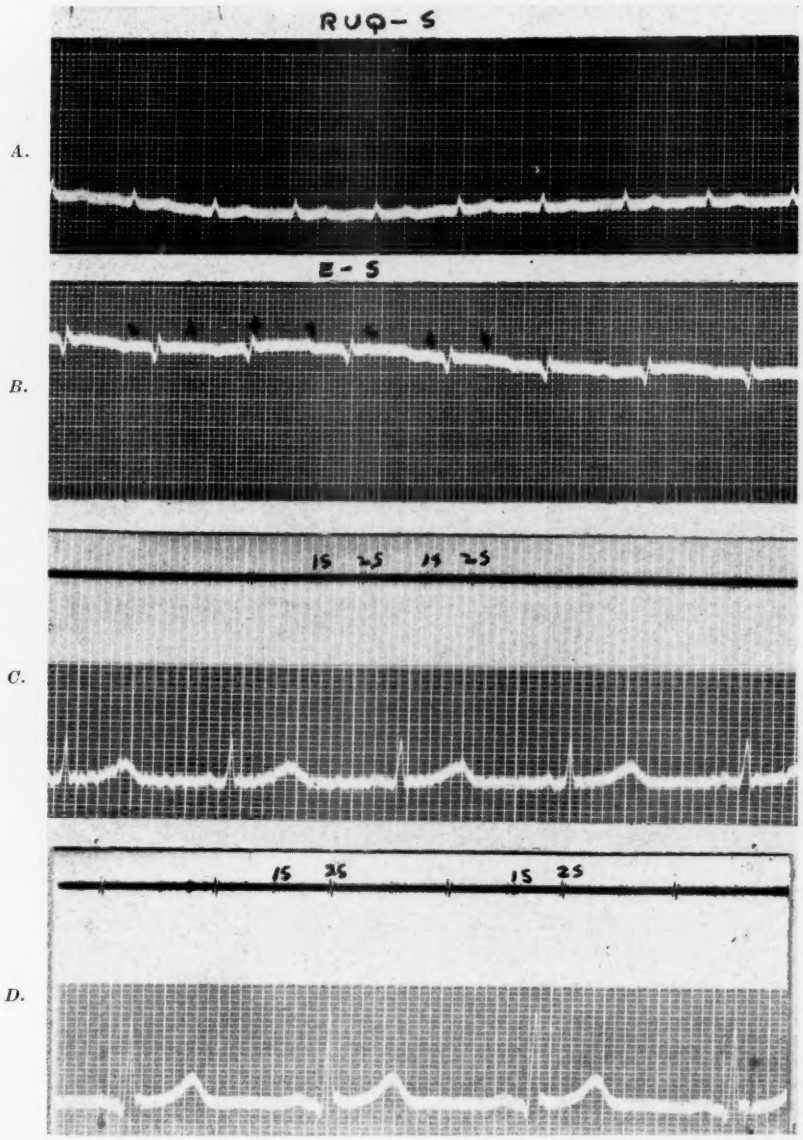

Fig. 3.—*A*, Case No. 13, 5 months gravid, fetal electrocardiogram: *B*, Case No. 20, 7 months gravid, fetal electrocardiogram; *C*, Case No. 15, 9 months gravid, fetal stethogram; *D*, Case No. 11, 5 months gravid, fetal stethogram; *F*, fetal electrocardiographic deflection; *1S*, first fetal heart sound; *2S*, second fetal heart sound.

Discussion

The result of our study has confirmed the observations of other investigators in the field. Positive fetal electrocardiograms are obtained

in a large percentage of cases even with a technique which is still imperfect. It is obvious now that with improved technique, particularly with regard to amplification, 100 per cent is not unlikely.

When this point is achieved, the practical value of fetal electrocardiography and stethography will be unquestioned. Viability of the fetus, pseudocyesis, multiple pregnancies, fetal arrhythmias and fetal distress will be diagnosed or confirmed by graphic methods. Perhaps even the subject of congenital cardiac lesions may come within the scope of these procedures.

It is of interest to note that there were less positive tracings obtained in the seventh and eighth months of gestation than in the fifth, sixth, and ninth. This is in accord with the findings of other observers. A possible explanation for this phenomenon is the relative increase of amniotic fluid during those two months. The weight of the mother, as well as the size of the fetus at the time of recording are apparently also factors in determining the production of fetal deflections.

An analysis of the fetal stethograms reveals that the concept of embryocardia is false in its implication. Embryocardia is commonly understood to mean equidistant heart sounds of equal intensity, quality and duration. This study proves that the fetal heart sounds differ from each other in a manner similar to those of the adult sounds. The first and second sounds are never identical in appearance in the same fetus. Similarly, diastole is longer than systole and approaches the latter in rapid rates.

Summary and Conclusions

1. An attempt was made to record fetal electrocardiograms and stethograms in 21 gravid women of varying periods of gestation.
2. Positive fetal electrocardiograms were obtained in 53 per cent.
3. Positive stethograms were obtained in 79 per cent.
4. Where large fetal electrocardiographic deflections were obtained they were diphasic, otherwise they were single downward spikes in all but one case. The latter was probably a breech presentation at the time the record was made.
5. The weight of the mother and size of the fetus influence the successful demonstration of the fetal electrocardiogram.
6. The age of the mother, her parity, fetal presentation and fetal sex are not factors in determining the production of fetal electrocardiographic deflections.
7. The fetal cardiac rate bears no relationship to its sex.
8. Limb leads are of no value in obtaining fetal electrocardiograms.
9. The best abdominal leads were those connecting the fundus of the uterus with the symphysis pubis.
10. The pattern of a fetal stethogram resembles that of the adult.
11. The configuration of the sounds assumes the form of M, N, or W.
12. The term embryocardia is a misconception.

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THROMBOCYTOPENIC PURPURA IN PREGNANCY

Review of the Literature With a Report of Three Cases

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PURPURA hemorrhagica is at best a rare disease, but its coexistence with pregnancy is rarer still. Hence, the admission of a Negress five months pregnant, who developed purpura hemorrhagica led to the review of the literature which follows. We shall consider purpura, first in general, and then its relationship to pregnancy.

Purpura is so inclusive a term that it is well to use Wintrobe and Rosenthal's classification, which is as follows:

I. Primary, Essential or Idiopathic
   1. Acute
   2. Chronic

II. Secondary or Symptomatic
   1. Blood diseases
      (a) Anemia, aplastic, hemolytic or caused by metastases to the bone marrow
      (b) Leucemia
      (c) Splenomegaly, Banti's disease or Gaucher's disease
   2. Infections, acute or chronic
      (a) Septicemia
      (b) Subacute bacterial endocarditis
      (c) Typhoid fever
      (d) Scarlet fever
      (e) Syphilis
      (f) Tuberculosis
   3. Intoxications
      (a) Quinine
      (b) Benzol
      (c) Snake venom
      (d) Sulfonamides
      (e) Ergot
      (f) Arsenicals
      (g) Mercuric bichloride
      (h) Gold salts
      (i) Belladonna
   4. Radiation
      (a) Radium
      (b) X-rays
   5. Jaundice
      (a) Hepatitis
      (b) Cirrhosis
   6. Chronic nephritis with nitrogenous retention
   7. Food sensitivity (Orris root, etc.)
   8. Vitamin deficiency (C, P and K)

III. Congenital

Symptomatic purpura while usually nonthrombocytopenic, may occasionally be thrombocytopenic, e.g., following arsenical treatment or exposure to x-ray. Though most of the cases which occur in pregnancy are of the symptomatic variety, we will confine our discussion to the primary type of thrombocytopenic purpura.

Purpura was first observed in pregnancy by Arand in 1765. Ten years later, in 1775, Werlhof described essential purpura for the first time. Almost a century elapsed till Barnes reported what is commonly considered the first case of purpura in pregnancy. In 1887, Denys first noted the absence of platelets in purpura and subdivided purpura into two types, thrombocytopenic and nonthrombocytopenic. Hayem, in 1896, discovered that patients with thrombocytopenic purpura had poor clot retraction. In 1911, Duke demonstrated that while the bleeding time was increased, the clotting time was normal. In 1916, Schloffer of Prague, at the insistence of Kaznelson, performed the first successful splenectomy for thrombocytopenic purpura. From 1920 to 1940, some 300 splenectomies have been done. Since that time, progress has been made in distinguishing essential from symptomatic purpura; in observing the effect of splenectomy and in experimenting with innumerable medical treatments.

Thrombocytopenic purpura is more common in women than in men. It usually makes its appearance in the first decade of life, or in the adolescence. In one series, 70 per cent of the patients were less than 24 years old, while in another 27 per cent of the patients were girls less than ten years of age. It is stated that under the age of ten and over 40, it is a mild disease with remissions. It is thought to be rare in the Negro, but in one series of 43 cases reported by Limarzi, there were three Negresses.

Theories concerning etiology are many, but they resolve themselves into two main types: (1) Defective production of platelets in the bone marrow; or (2) increased destruction of platelets by the spleen. Limarzi champions the former theory, stating that thrombocytopenic purpura is due to faulty maturation of the megakaryocytes in the bone marrow, and that splenectomy cures the disease by removing a factor which is inhibitory to their proper maturation. Frank and Kaznelson hold to the latter opinion. Frank believes that the spleen produces a myelotoxic substance, which by causing a decreased production of megakaryocytes, results in fewer platelets. Kaznelson also believes that thrombocytopenic purpura is due to thrombolytic activity of the spleen. He adduces the following evidence: (1) Megakaryocytes are present in the blood and bone marrow in normal amounts prior to splenectomy and, (2) platelets increase after splenectomy. A thrombocytolytic substance has been postulated by some investigators. In 1938, Troland and Lee reported that intravenous injection of acetone extracts of spleens removed from patients with thrombocytopenic purpura reduces the number of platelets in the circulating blood of rabbits. There

is a rapid fall in the platelets, and an even sharper return to normal in 48 hours. Despite the fall in the platelets, there are no hemorrhagic manifestations. Jerome similarly reported a transient significant depression in the platelet count, but not on the bone marrow or the megakaryocytes. Other observers, such as Paul and Uihlein, have failed to demonstrate, or disprove the existence of such thrombocytolytic substances.

Platelets are formed by budding from the cytoplasm of the megakaryocytes in the bone marrow. They are spheric or ovoid, granular bodies about two to four microns in diameter with a life expectancy of three to five days. By producing thromboplastin, they initiate clotting. The normal number in the blood is 200,000 to 400,000/cubic millimeters. Forty thousand is regarded as the hemorrhage level. After a splenectomy, the level of platelets rises to normal in 24 to 48 hours. From then on it may be supernormal, or may fall slightly below normal. Thrombocytopenic purpura is believed by Whitby and Britton to be due to (1) quantitative deficiency of the platelets caused either by primary defect of platelet formation, or pathologic destruction in the spleen or, (2) qualitative deficiency of the platelets. It is not due to the small number of platelets because patients with low platelet counts may not bleed. Further, the bleeding is not due to the increased bleeding time because this is not invariably present. Though there is no convincing evidence that it is due to the capillary bed, Brill and Rosenthal feel that the changes in the platelets cause changes in the capillary walls, while McFarlane states that in thrombocytopenic purpura the capillaries have malformed loops, damaged endothelium and defective contractility. So, at present, there is no adequate explanation as to why patients with thrombocytopenic purpura bleed.

Yet, despite this lack of explanation, bleeding is the chief symptom of thrombocytopenic purpura. The patient usually comes to the doctor complaining of bleeding from the mouth, or epistaxis, or hematuria. The acute phase is more common in early life and the patient may progress to death from anemia or intracranial hemorrhage. This latter is the most feared complication and may result in hemiplegia, meningitis or death. Recovery from the acute attack occurs in two weeks to several months. From then on the disease may be chronic with remissions and exacerbations.

The most striking physical sign is the presence of purpuric spots varying in size from the point of a pen to the head of a pin. They may even increase in size until they become ecchymoses. Clotted blood may be seen at the nares, or the gum margins. Infection of the mouth, with Vincent's organisms is a common association. The liver and spleen are rarely enlarged. Most authorities agree that the spleen is palpable in less than one-third of the patients with thrombocytopenic purpura and further state that if the spleen is enlarged, the disease is more likely a symptomatic purpura.

The diagnosis is confirmed by the platelet count. This is the only constant laboratory feature. Whereas the platelets are normally 200,000 to 400,000/cu. mm., they are less than 100,000 and may even be absent. The second most important laboratory measure is aspiration of the sternal bone marrow. Normally mature megakaryocytes are present, while in thrombocytopenic purpura the bone marrow is normal, or there is a megakaryocytic hyperplasia. Some authors state that there exists a uniform stimulation of all the elements of the bone marrow with myeloid, erythroid and megakaryocytic hyperplasia. Immature megakaryocytes with hyalinization and vacuolization of the cytoplasm, and degenerative types of nuclei are seen. This test excludes metastases, aplastic anemia and the leucopenic phases of leucemia. Prolongation of the bleeding time is the third distinguishing characteristic. By Duke's method, this is normally one to three minutes. It may in thrombocytopenic purpura, however, be prolonged from ten to ninety minutes or strangely enough, may be normal. Clot retraction normally begins in one to two hours and is complete in 18 to 24 hours, while in thrombocytopenic purpura a soft clot forms which often shows no tendency to retract in 48 hours. In thrombocytopenic purpura petechia usually occur after the Rumpel-Leede test, the so-called capillary resistance test, whereas normally they do not. The clotting time, which by the Boyce-McFettridge technique is normally 8 to 10 minutes, is normal. The white blood count may be normal, or there may be a leucocytosis. The degree of anemia is proportionate to the blood loss. Blood levels for calcium, fibrinogen, vitamin C and prothrombin are normal.

Thrombocytopenic purpura must be distinguished from a host of diseases. The chief of these, symptomatic purpura of the nonthrombocytopenic variety, whether due to allergy, infection or idiosyncrasy to food or drug, is readily distinguished by its normal platelet count, normal bleeding time and the presence of clot retraction. Hemophilia is differentiated because there is usually a familial history which does not exist in thrombocytopenic purpura; the bleeding in hemophilia is caused by trauma; the bleeding time is normal, the clot retraction and the platelet count are normal while the clotting time is prolonged. Thrombocytopenic purpura is readily distinguished by laboratory data from acute aplastic anemia in which there is deficiency of all the formed elements of the blood, and from acute leucemia in which immature white blood cells are present in the bone marrow and the blood smear. Lack of vitamin C, commonly called scurvy, and deficiency of vitamin K may be readily excluded by obtaining blood levels for the respective vitamins. A few rarer diseases, such as familial epistaxis, hereditary hemorrhagic telangiectasia, polycythemia vera, lupus erythematosus disseminatus, von Willebrand's thrombopathy or Glanzmann's hemorrhagic thrombasthenia are distinguished by the absence of the blood findings characteristic of thrombocytopenic purpura.

TABLE I. CRITERIA FOR THE DIAGNOSIS OF ESSENTIAL THROMBOCYTOPENIC PURPURA

	NORMAL	THROMBOCYTOPENIC PURPURA
Platelet count	200,000/cu. mm. 400,000/cu. mm.	Less than 100,000/cu. mm. May be entirely absent Only constant abnormality
Bleeding time (Duke's method)	1 to 3 minutes	10 to 90 minutes This may be normal
Capillary resistance test (Rumpel-Leede)	No petechiae	Petechiae
Sternal puncture	Normal	Megakaryocytic hyperplasia
Clot retraction	Begins in 1 hour, complete in 24 hours	May not begin in 24 hours
Anemia	None	Normocytic, proportionate to the bleeding
Clotting time (Boyce-McFettridge Method)	10 minutes	Normal
Vitamin C	0.8 to 1.2 mg. %	Normal
Vitamin K (Werner, Brinkhous Smith)	100%	Normal
Abnormal cells in bone or blood	None	None

Treatment

The treatment of thrombocytopenic purpura is both medical and surgical. In the acute phase, the patient is placed in bed, a high protein and high vitamin anti-anemic diet is given and Feosol is administered. In accord with the recommendations of Squire and Madison, foods to which the patient might be sensitive are eliminated from the diet. Blood, citrated and fresh, or red cell transfusions are given to control the bleeding, to keep the red cell count above 2,000,000 and to keep the blood pressure above 90. Moccasin venom, in dosage of 0.4 to 1.0 c.c. of 1 to 3,000 solution may be given subcutaneously twice weekly. This, however, is without proved effect. High voltage x-ray, ultraviolet rays, calcium, vitamin C and parathyroid extract have been given, but most authors agree that they are of little value. Within the past year citrus pectin, in dosage of 3 to 9 grams a day has been recommended by Isaacs. This checks the bleeding without affecting the platelet count. Either spontaneously or because of the above therapy, the acute phase will subside. In this interval, foci of infection are removed or splenectomy is done. Splenectomy may also be done during an acute episode which fails to respond, but here the risk is greater. The primary mortality of splenectomy in thrombocytopenic purpura varies from 5 per cent as recorded by Wiseman to 13 per cent as reported by Walton. The preoperative preparation includes multiple transfusions and the demonstration of a hyperplastic bone marrow. If the bone marrow is aplastic, splenectomy is of no value inasmuch as we are more likely dealing with an aplastic anemia, or a leucopenic leucemia rather than an essential thrombocytopenic purpura. Splenectomy is contraindicated if there is any doubt of the diagnosis, if there is a history of recent drug ingestion and, above all, if sternal puncture

fails to reveal megakaryocytes in the bone marrow. The indication for splenectomy is a recent exacerbation of thrombocytopenic purpura which has not subsided, or an acute phase which fails to respond to medical treatment. The curative value of splenectomy in thrombocytopenic purpura is dramatic. Bleeding ceases as the splenic pedicle is ligated. The platelets sharply rise to normal in 24 to 48 hours as was shown by Brown and Elliott, then reach a peak in ten days and may later show a secondary fall. Postoperative pneumonia and atelectasis are frequent because of the intimate connection of the spleen to the adjacent thorax. Sometimes, however, splenectomy fails. This is due to incorrect diagnosis, to the presence of accessory spleens, or to a hypoplastic bone marrow.

During the acute exacerbation the prognosis is guarded. However, when the patient is less than ten years or over 40, remission occurs rapidly. The presence of hematuria is reputed to be ominous because death usually follows. At autopsy, the capsules of the kidney glomeruli are found filled with blood. From our experience this seems to be an overstatement. The development of signs of intracranial injury is also alarming. Death is usually due either to the blood loss or to the brain hemorrhage. At autopsy, the only constant feature is hemorrhage, both gross and microscopic. The bone marrow may be normal, or may show megakaryocytic hyperplasia. The lymph nodes are not enlarged. The spleen, whether removed at operation or at post mortem, is rarely enlarged but is hyperplastic. Meningitis may be superimposed on intracranial hemorrhage.

Because of its rarity, little is known about thrombocytopenic purpura in relation to pregnancy. While there is no way to estimate the number of unrecorded cases, Long states that 80 cases of purpura in association with pregnancy have been reported. Burnett and Klass in December, 1943, however, could find records of only 68 cases. Forty-six of these they considered as doubtful, 18 they regarded as representing symptomatic purpura, and only four were true thrombocytopenic purpura. Then they described in detail their case which they regard as the fifth true case of thrombocytopenic purpura recorded in the literature. On an analysis of these five cases, Burnett and Klass believe that there is no causal relationship between thrombocytopenic purpura and pregnancy, but rather that thrombocytopenic purpura has periodic lapses which may coincide with pregnancy. They state that it is equally common in multiparas and primiparas, while Mosher believes that it is more common in multiparas. Burnett and Klass further state that only one out of five patients had hemorrhagic tendencies prior to the pregnancy, and that they were normal in previous pregnancies. They further believe that thrombocytopenia develops early in pregnancy while Mosher thinks that it occurs most frequently in the second half of pregnancy. Most authors agree that no hemorrhage occurs at the time of delivery, though Mosher and also Hirst state that all cases of purpura end fatally because of hemorrhage.

Perhaps the best method of learning of the relationship of thrombocytopenic purpura to pregnancy is to narrate the few cases which have been recorded. We shall first describe the five cases which Burnett and Klass accept as being true thrombocytopenic purpura, add five more from the literature, and then report in detail the three cases which have been observed at the New York Hospital. The first of the five cases accepted by Burnett and Klass was reported by Liebling in 1926. A 22-year-old primigravida, who, when first seen in the seventh month of pregnancy, complained of bleeding from the nose and gums since the fifth month. In the sixth month the platelet count was 40,000 but one month later it rose to 300,000. An 8-pound, 11-ounce baby was delivered in whom petechiae were present and whose vomitus, urine and stool were blood stained. By the fifth postpartum day, the infant's symptoms had ceased while the mother was cured two months post partum. Siegler, in 1934, reported regarding a 29-year-old para iii, gravida v who had had purpura for the past seven years, who had had a hemorrhage after a menstrual period two years ago, and who had a postpartum hemorrhage at the last delivery. There were purpuric spots over her entire body, and her platelet count was 80,000. At delivery, the blood loss was 1,500 cubic centimeters. A 10-pound, 10-ounce infant was delivered and died on the fourth postpartum day of an unstated cause. Unfortunately, no post mortem was performed. In 1935, de Saussure and Townsend decribed a 35-year-old Negress, para viii, gravida ix, who at term had hematemesis, vaginal bleeding and hematuria. The next day, a stillborn infant was delivered. At the time of the delivery, the mother's platelet count was 33,000 and the bleeding time 30 minutes. The platelets at the time of discharge were 144,000. The fourth case was reported in 1939 by Bernstein, Newman and Hitzig. In early pregnancy, purpura of the skin appeared; in the fifth month, vaginal bleeding and epistaxis occurred. The platelet count was 10,000, the tourniquet test was positive, and the bone marrow was normal. The patient was treated by transfusions and splenectomy at which time a hyperplastic spleen was removed. Postoperatively, the bleeding stopped and the purpura disappeared. A 1,400-gram infant, who was free of purpura was delivered and died on the eighth day of atelectasis. At post mortem, the infant's hematopoetic system was normal. In the last case, Burnett and Klass's own, a primigravida had epistaxis and petechiae in the fourteenth week of pregnancy. The platelet count was 15,000; the bleeding time, 27 minutes; the clotting time, four minutes; the tourniquet test positive and the clot retractility normal. Spontaneous remission occurred and a 3,600-gram infant, who was normal, was delivered with little blood loss.

In addition to these five cases, there are five other cases which represent thrombocytopenic purpura. Hottenstein and Klingman, in 1927, described a 30-year-old, para i, gravida ii, who had a postpartum hemorrhage with her first delivery. When she was six months pregnant, purpura of the trunk and extremities appeared. The platelet count was

25,000. Transfusions were given and a 3,320-gram infant, who was well 8 months post partum, was delivered. By the seventh postpartum day, the mother's hemoglobin had fallen to 10 per cent. A splenectomy was done with death occurring on the second postoperative day. The autopsy revealed acute endometritis and subcutaneous hemorrhage. Limarzi, in 1940, reported another case which is undoubtedly thrombocytopenic purpura. Though purpuric spots had been present for a year prior to pregnancy, bleeding from the nose and mouth did not occur until the seventh month. After several transfusions, a spontaneous delivery of a 6-pound, 8-ounce infant occurred. There was no hemorrhage; the child was normal, and a splenectomy was done one month post partum. A third case, which is not included by Burnett and Klass, is reported by Phythyon and Lartz in 1943. A 28-year-old primigravida when seven months pregnant bled from the gums, had hematuria and purpura. The bleeding time was increased; the platelets were 68,000. After three transfusions, a splenectomy was done. On the second postoperative day, a premature stillborn infant was delivered. By the twelfth postoperative day, the platelets were normal, 240,000.

Troland and Lee describe a fourth case of a 22-year-old woman who, in August, 1936, noticed bleeding from her gums. Her blood studies were normal until in December, there was some reduction in platelets. On January 27, 1937, a normal child was born, the blood loss being 150 cubic centimeters. At the time of delivery, the platelets numbered 78,000, bleeding time was 8 minutes and the tourniquet test was positive. Throughout the next two months, vaginal hemorrhage occurred until in April, a splenectomy was done. All symptoms regressed after this, and the blood studies were normal.

A fifth case culled from the literature was reported by Polowe in March, 1940. This patient was a para i, gravida ii, who had had purpura during her first pregnancy which had occurred five years ago. In the first pregnancy the infant was normal, and apart from the need for two transfusions, the pregnancy was uneventful. In the sixth month of the second pregnancy ecchymoses, epistaxis, hemoptysis and hematuria occurred. The platelet count was 60,000, the bleeding time 12 minutes, the clotting time 11 minutes and the tourniquet test was positive. In the eighth month of pregnancy, a splenectomy was done. The spleen weighed 1,060 grams and was described as a splenoma with necrosis. About a month later, a normal baby was delivered. The author asserts, "I believe this is the first case to be reported of splenectomy in pregnancy complicated by thrombocytopenic purpura hemorrhagica." However, in 1939, Bernstein, Newman and Hitzig, and in 1943, Phythyon and Lartz, reported the performance of splenectomies during pregnancy for thrombocytopenic purpura. Also in a letter in the *Journal of the American Medical Association* in May, 1944, Grossman states that Garlock performed a splenectomy "a few years ago" for thrombocytopenic

purpura occurring during pregnancy. Doubtless there are other unreported cases. Two additional cases reported by Sanford, Leslie and Crue, and Urbanski and Hutner most likely represent thrombocytopenic purpura, but the evidence is not sufficient to warrant this conclusion.

Case Reports

From September, 1932, to June 1, 1944, 43,334 pattients have been delivered in the New York Hospital. Three of these had thrombocytopenic purpura.

CASE 1.—P. S., a 17-year-old Negress. Her last menstrual period was August 22, 1943, making the expected date of confinement May 29, 1944. Since 1934, at the age of seven, she had had repeated episodes of bleeding from the gums. In 1934, the platelet count was 6,400. Until 1941, she improved on rest and transfusions but at this time, after failure to improve and with decrease of the platelet count to 32,000, splenectomy was done. Her improvement was only gradual, and she had several episodes of bleeding from the gums during the first postoperative month. In the fifth month of pregnancy, in 1944, three years after the splenectomy, she again noted bleeding from gums, dizziness, fatigue and dyspnea. When examined, purpuric spots were present, and there were clots of blood about the gum margins. Smear from the mouth contained Vincent's organisms. After several transfusions of red cells, feosol, citrus pectin and a high vitamin diet, the patient improved so much in the course of two weeks that she was followed in the antepartum clinic and the hematology clinic.

She continued in good condition on the above-mentioned routine until May 7, when bleeding from the gums again occurred. An examination of the urine revealed hematuria, hence she was readmitted. Transfusions, ferrous sulfate, citrus pectin in increasing doses were given with marked improvement for two weeks, but then an exacerbation of the disease occurred with marked bleeding from the gums, and hematuria. On June 9, 1944, a full-term spontaneous delivery of a 3,520-gram female infant occurred. Blood loss was 50 cubic centimeters. Bleeding from the gums stopped almost immediately after delivery, but blood destruction continued as indicated in the following chart. Her puerperium was marked by a low-grade fever due to intrauterine infection with *Bacillus aerogenes* and anaerobic nonhemolytic streptococcus, and a urinary tract infection caused by *Bacillus aerogenes*. Sulfonamide therapy was deemed unwise so 600,000 units of penicillin were given with good effect. The remainder of the puerperium was uncomplicated by bleeding or fever.

The female infant weighed 3,520 grams. As no signs of purpura developed, and analyses of blood and spinal fluid revealed no evidence of internal bleeding, the infant was discharged with her mother.

CASE 2.—D. C., noticed gastric hemorrhage when she was six and had profuse menses at 14 in 1930. She then showed petechiae of the arms and legs. Prior to splenectomy which was done on April 29, 1930, the platelet count was 20,000, the bleeding time was 30 minutes, and there was delay in the clot retraction. Postoperatively, the platelet count was 100,000 and the bleeding time was 10 minutes. Subsequently, there was no bleeding tendency. In the first pregnancy, in 1939, purpuric

TABLE II. LABORATORY DATA OF MOTHERS

	ANTE PARTUM					DAY OF DELIVERY	POST PARTUM	
	2/2/44	2/14/44	5/8/44	5/15/44	5/26/44	6/9/44	6/12/44	6/19/44
Hemoglobin	5.1 grams	11.5 grams	11.0 grams	13 grams	11.0 grams	8 grams	6.5 grams	11.0 grams
Red blood count	2,400,000	4,400,000	4,000,000	5,200,000	4,400,000	2,700,000	2,300,000	3,500,000
White blood count	16,000			9,500	10,700			10,150
Icteric index	3		3	3	3			1.1
Volume index	0.84		0.88	0.91	0.95	0.97		1.1
Color index	0.79		0.94	0.86	0.91	1.03		1.07
Platelets	130,000	460,000	70,000	220,000	110,000	140,000		130,000
Bleeding time	27 minutes	2.5 minutes	11 minutes	1½ minutes	12 minutes	10+ minutes	6 minutes	15 minutes
Clotting time	5 minutes	9.5 minutes	9 minutes	11 minutes	11 minutes	11 minutes	9 minutes	11 minutes
Clot retraction	13% serum in 7 hours	10% serum in 4 hours	None after 4 hours	32% serum in 4 hours	None after 4 hours		52% serum after 4 hours	2% after 4 hours
Fragility	Fair		Poor	Poor	Very poor		Fair	Poor
Tourniquet	1 Petechia/7 minutes	None	Neg. after 7 minutes	Neg. after 7 minutes			Negative	Neg. after 7 minutes
Prothrombin	69%	80%	40%	50%	96%		41%	76%
Vitamin C	0.73 mg. %	0.45 mg. %	0.76 mg. %	0.34 mg. %	0.56 mg. %		0.5 mg. %	0.5 mg. %
Blood type	B							
Rh	Negative							
Sedimentation rate	0.75							
Calcium	10.00 mg. %							
Chemistry	Normal							
Reticulocytes		3%		3%	1.1%		6.2%	

TABLE III. LABORATORY DATA OF INFANTS

	6/10/44 BIRTH	6/13/44 3 DAYS	6/19/44 9 DAYS
Hemoglobin	16.5 Gm.	14.5 Gm.	
Red blood cells	7,100,000	3,800,000	
White blood cells	15,300	8,000	
Platelets	290,000	160,000	235,000
Nucleated red blood cells (per 100 white cells)	5	8	
Prothrombin		88%	
Bleeding time	3.5 minutes		1 minute
Clotting time	16 minutes	4 minutes	4 minutes
Clot retraction	Almost complete in 6 hours	Normal	

spots were present but all blood tests were normal. There were occasional nosebleeds one month prior to term, and the platelet count fell to 45,000. Blood loss at delivery was 60 cubic centimeters. The infant weighed 3,100 grams. About five hours after birth, many petechiae appeared on the infant's extremities. There was a cephalohematoma on the right parietal area. The petechiae spread until they covered the entire body. The platelet count was 120,000; the red cells numbered 5,400,000; the bleeding time was greater than 7 minutes and the clotting time was 3 minutes. The infant began to vomit blood-stained mucus. Despite many transfusions, the infant died on the third day. The autopsy revealed jaundice, subaponeurotic hemorrhage of the head, subarachnoid hemorrhage, hemorrhage into the subcutaneous tissue, and petechiae of the thymus and visceral pleura. In 1941, a spontaneous abortion occurred at 3 months. In the third pregnancy, in 1942 to 1943, when three months pregnant, platelet count and bleeding time were normal, but the tourniquet test showed numerous petechiae. At delivery, the blood loss was 100 cubic centimeters. A 3,300-gram baby was delivered in whom purpura developed one hour after delivery, but in whom no bleeding occurred. The platelet count was 40,000; bleeding time was more than 90 minutes; clot retraction was absent and sternal aspiration showed a decreased number of megakaryocytes, and failure of production of platelets. After multiple transfusions the child improved. Six weeks after delivery no bleeding had occurred, the purpuric spots had disappeared and the bleeding time was 3 minutes. There is no further follow-up on the patient.

CASE 3.—S. A., in 1935, at 17 years of age, had an induced labor in the seventh month because of eclampsia. In the second pregnancy, in 1936, though partial premature separation of the placenta occurred, a living 1,500-gram baby was delivered. In December, 1941, the patient noticed bleeding from the gums, vaginal hemorrhage and ecchymoses. At this time, the platelet count was 10,000, bleeding time was over 30 minutes, clot retraction was defective, while the tourniquet test was positive. The bone marrow was normal. A splenectomy was done on January 8, 1941. All bleeding ceased and the platelets rose to 360,000. The postoperative course was complicated by atelectasis and bronchopneumonia of the left lower lobe. The spleen was unremarkable. In the fifth month of the third pregnancy (August, 1943), the platelets were 520,000 and the bleeding time was one minute. In January, 1944, a 3,560-gram infant was delivered, the blood loss being 450 cubic centimeters. Both infant and mother were discharged well.

Discussion

How is the child affected by the thrombocytopenic purpura of the mother? Some answer has already been given by the case reports. A great variance of opinion exists. Mosher states that 50 per cent of the infants die in utero, or after delivery. Burnett and Klass, at the other extreme, believe that if the fetus develops purpura, it is not essential thrombocytopenic purpura but is symptomatic purpura, or is due to familial platelet defect. Rushmore, in 1925, reported seven instances in which purpura was present in both mother and child. Our second case will add two more examples of this, the first baby dying of congenital thrombocytopenic purpura, the second living and also regarded as an example of congenital thrombocytopenic purpura.

Walton states that if the blood picture of the purpuric mother shows a complete remission after splenectomy, the newborn will be free from thrombocytopenic purpura. Our third case illustrates this. Wiseman, Doan and Wilson believe that while thrombocytopenic purpura is often congenital, there is no proof that it is inherited. Whiting and Barritt report a woman who had a splenectomy at the age of 14, and who 10 years later had two babies, both of whom developed purpuric spots and died within three days after delivery of intracranial hemorrhage. They assert that these cases represent congenital thrombocytopenic purpura rather than hemorrhagic disease of the newborn because of (1) the immediate spontaneous appearance of the hemorrhage, (2) the normal prothrombin level of the second baby, (3) the fact that neither infant responded to whole blood and (4) the fact that vitamin K was given antenatally and to the baby after birth. Just what the prognosis of the baby is, is difficult to state but from an analysis of the ten cases reported, it would appear better for the infant if the disease is in a chronic phase, and if a splenectomy has been done prior to the pregnancy.

TABLE IV. OUTCOME IN INFANTS

N.Y.H.	DIED	LIVED
Case 1	1 (Congenital thrombocytopenic purpura)	1 (Congenital thrombocytopenic purpura)
Case 2		1 (Normal)
Case 3		1 (Normal)
Literature		
Case 4		1 (Bled until the fifth day)
Case 5	1 (Died on the fourth day. No autopsy obtained)	
Case 6	1 (Stillborn)	
Case 7	1 (Post splenectomy. Died on the eighth day of atelectasis and prematurity)	
Case 8		1 (Normal)
Case 9		1 (Normal)
Case 10		1 (Normal)
Case 11	1 (Stillborn, postsplenectomy)	
Case 12		1 (Normal)
Case 13		1 (Normal)

Summary

Thrombocytopenic purpura has been discussed both as a disease entity and in relation to obstetrics. In addition to the five cases which are regarded by Burnett and Klass as true purpura, eight more have been added—five of these from the literature, and three from the New York Hospital records.

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A STUDY OF COMMERCIALLY MANUFACTURED CATAMENIAL TAMPONS*

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PART I

IN RECENT years, there has been a very marked increase in the use of commercially manufactured tampons for the control of women's menstrual flow. The purpose of this study was to investigate various types of commercial menstrual tampons with respect to their anatomical correctness, and the protection and comfort provided to the wearers. To make the study as generally helpful as possible, many factors were considered, and a great number of women were examined before the subjects were finally selected. Women of marked pathology were excluded and those finally chosen included women of various pelvic types and engaged in diverse occupations. The study makes final report on 25 women although many more cooperated in the work. No case has been reported unless the women were tested with at least two different tampons. Some of the women were not able to cooperate fully during the entire time, although they were seen at intervals during the course of the investigation. Three of them were tested for 7 months, 2 for 5 months, and the remainder from 1 to 4 months. Of the 25 women finally included, 12 have been rechecked within a year, and not one has shown any unfavorable effect from the use of tampons. During the period of this study, one woman was operated upon for a condition which existed before she ever used tampons, 5 women became pregnant —all primiparas—of whom 3 were delivered before the conclusion of this study.

All of the women were subjected to a routine examination. Urethral and cervical smears were taken and examined, but no cases of gonorrhea were discovered. The vaginal secretions were examined for *Trichomonas* vaginalis by the hanging drop method, and all examinations were found to be negative. A study of the vaginal epithelium was undertaken. The vaginal smears revealed normal epithelial cells to be present in all. Vaginal pH was determined by B.D.H. Universal Indicator and found to range from 3.0 to 5.5.

The women were questioned as to their previous usage of tampons—whether they had experienced discomfort, as defined to mean "an awareness of the tampon within the vagina," or "burning," defined as "the uncomfortable sensation at the introitus" which is noted more frequently when no inserter is used, or when the inserter is used without water or other lubricant to minimize friction during insertion. Of the

*This study was made possible by a grant from The Personal Products Corporation.

9 women who had previously used tampons, 7 had used tampon No. 7, 1 tampon No. 5, and 1 tampon No. 1. Of those using tampon No. 7, 5 reported discomfort, as did the woman using tampon No. 5, and 2 reported "burning."

Of the 25 women, 16 classified their menstrual flow as "moderate," 5 "heavy," 2 "heavy at first" and 2 "scant." When an attempt was made to correlate the individual woman's estimate of the amount of flow with the number of pads or tampons used, it became obvious that the description was often inaccurate. Conclusive results could be obtained only from correlating the length of adequate protection with the actual weight of the absorbed menstrual blood within the pad or tampon.

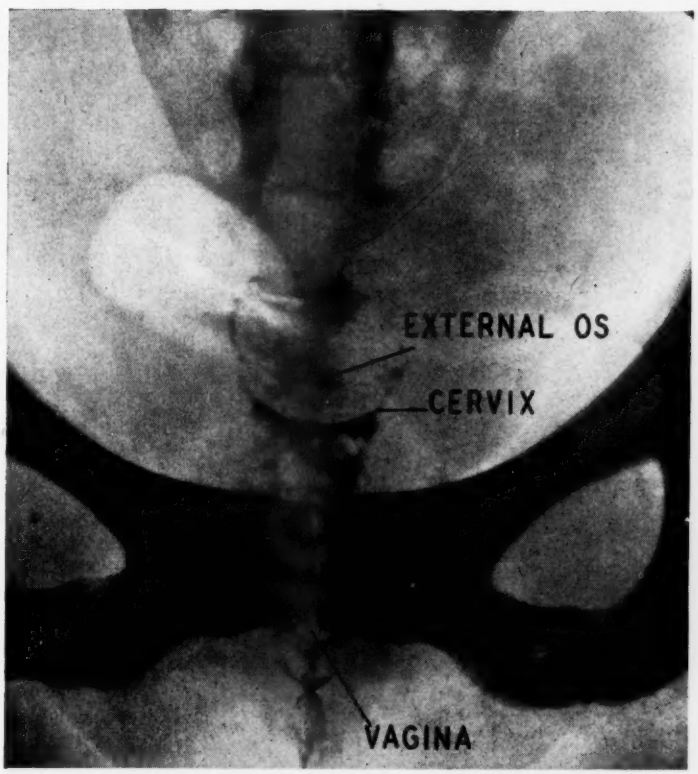

Fig. 1.—Tampon 1, after application of sodium tetraiodophenolphthalein, showing cervix and the vagina.

Studies of Commercial Tampons

Commercially manufactured catamenial tampons are of two general types. The first are those which are inserted by the user without the aid of an inserter. The other type is placed inside the vaginal tract with the aid of an inserter. Some tampons are not compressed for use, and some have been compressed to a smaller size so that they are inserted in the compressed size and expand within the vaginal canal as they absorb the menstrual flow.

The tampons numbered 1, 2, 3 and 4 in this study are those designed to be inserted without the use of a mechanical inserter.

Tampon No. 1 looks like a soft cotton ball. Its outer measurements* are 1⅜ inches by 1⅜ inches by 1⅜ inches, and it consists of two loosely, spirally wound cotton balls separated by 8 layers of surgical gauze. The whole is fastened to-

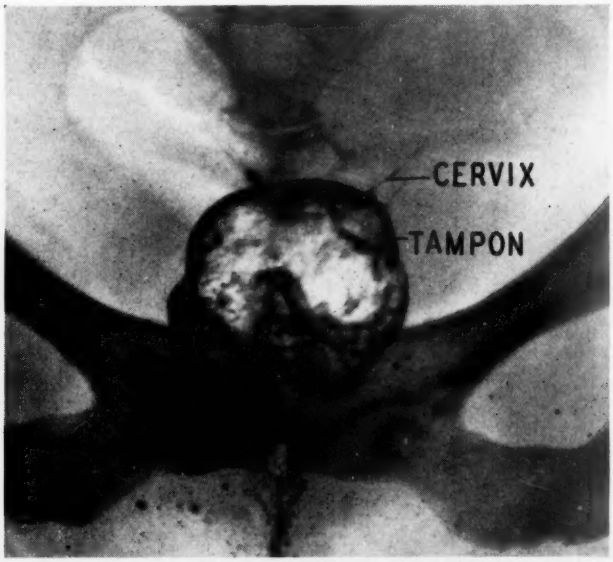

Fig. 2.—Tampon 1, showing tampon in position after insertion.

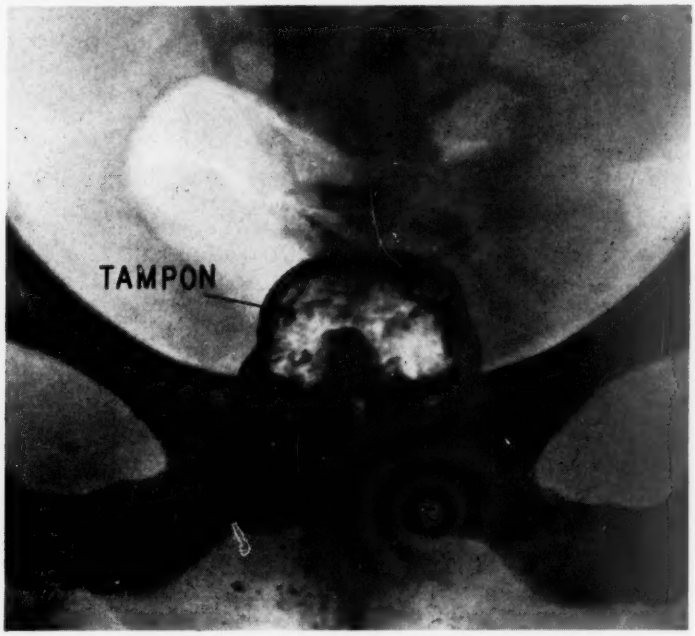

Fig. 3.—Tampon 1, showing tampon in position 20 minutes after insertion.

*Tampon dimensions given are those obtained at the time of the study.

gether by means of a waterproofed cord with double ends which hang loosely for a distance of about 5 inches, and which provide for the removal of the tampon. The surface of tampon No. 1 is soft, and pieces of cotton slough off on very slight handling. It is wrapped individually in cellophane, and according to the manufacturer's leaflet, is sterilized after being wrapped.

Fig. 4.—Tampon 2, shows tampon in vagina immediately after insertion.

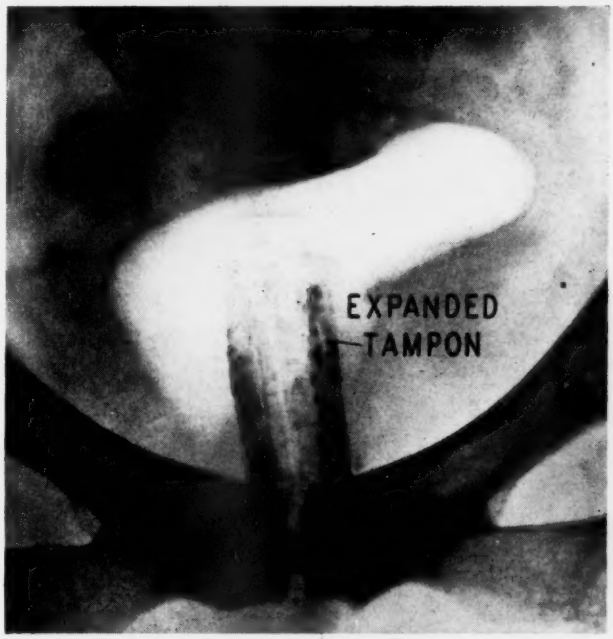

Fig. 5.—Tampon 2, shows expanded tampon 30 minutes after insertion.

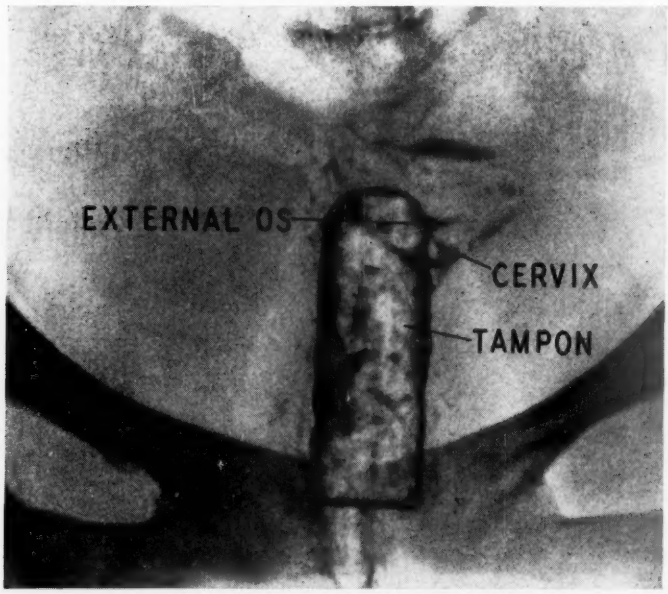

Fig. 6.—Tampon 3, shows tampon in vagina immediately after insertion.

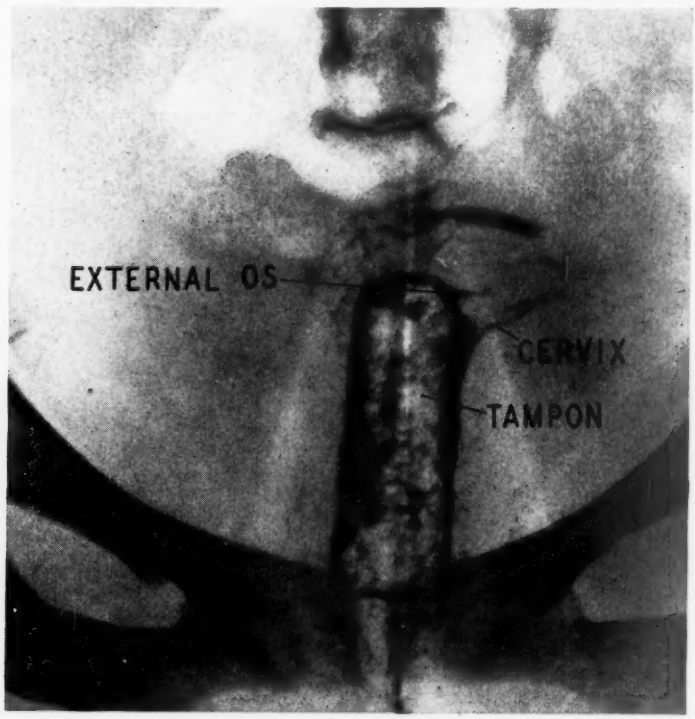

Fig. 7.—Tampon 3, shows tampon 20 minutes after insertion.

Tampon No. 2 consists of a strip of surgical cotton, approximately 2⅛ inches in width and 7 inches in length, that is wound on itself with a string in its core to produce a loosely wound roll, approximately ¾ of an inch in diameter and 2⅛ inches in length. Lateral compression on 6 sides results in a final diameter of ⅜ of an inch with no alteration of the length by compression. The tampon ready for use measures 2⅛ inches in length and ⅜ of an inch in diameter. Both the pointed end and base are somewhat rounded. This tampon is wrapped in cellophane in packages of 2 and 4.

Fig. 8.—Tampon 4, shows tampon 20 minutes after insertion.

Tampon No. 3 is individually wrapped in cellophane and is nonextending. It measures approximately 2⅛ inches in length and 9/16 of an inch in diameter, and has a draw string anchored by means of a chain-lock stitch about ¼ of an inch from the base which permits 3½ inches to hang free for removal. The pointed end is well beveled, covered with a sizing substance, to anchor the "quilting" threads which interlace diagonally along the sides of the base. There are two layers of "quilting" threads one on the outside overlying the thin layer of cotton which itself covers a core consisting of a roll of cellulose, bound together by the other layer of "quilting" threads. The base of this tampon is square cut.

Tampon No. 4—this is an uncompressed type of tampon that measures 2¼ inches in length and ¾ of an inch in diameter. It consists of a roll made from a strip of surgical cotton approximately 8½ inches in length and 2⅜ inches in width. The pointed end is well beveled and coated with a sizing substance to aid in the maintenance of shape and smoothness. A strip of cellophane 1⅜ inches in width is wrapped around the body of the tampon and anchored about ¼ of an inch from the base edge by means of a draw string. The cellophane strip is perforated by

numerous holes 1/16 of an inch in diameter. The base of this tampon is square cut and the draw string is well anchored with a chain-lock stitch placed about a half inch above the base of the tampon, allowing the ends of the string to hang free for approximately 3½ inches.

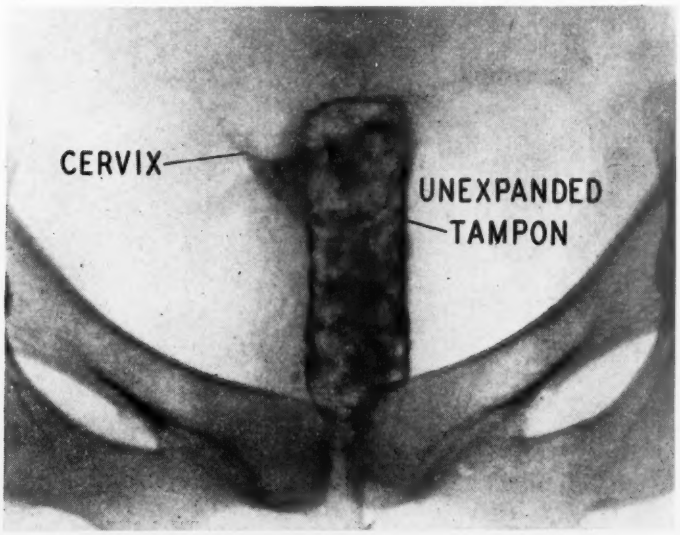

Fig. 9.—Tampon 7, shows tampon in vagina immediately after insertion.

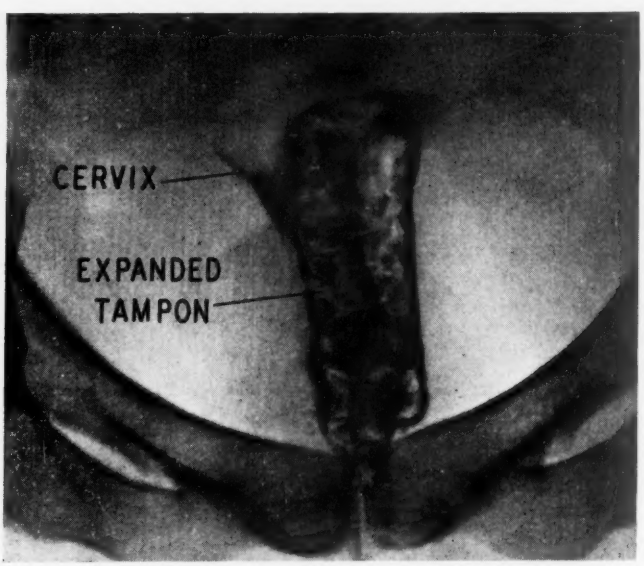

Fig. 10.—Tampon 7, shows tampon 40 minutes after insertion, showing expansion.

Tampons No. 7 and No. 12 are compressed tampons packed in mechanical inserters designed to place the tampon within the vaginal canal.

Tampon No. 7—this tampon is individually wrapped in cellophane and comes in three sizes—junior, regular and super. In this study, the regular size is considered as an average to compare with the other tampons which come in one size only.

The inserter consists of two tubes of highly glazed paper telescoping within each other. The outer tube is 2¾ inches in length and 9/16 of an inch in diameter. The inner tube is 3 inches in length and ½ of an inch in diameter. The tampon consists of a strip of surgical cotton approximately 1¾ inches in width and 4 inches in length. Through the length of the tampon, there is a cord sewn in by means of a lock stitch. Compression in two directions produces a tampon approximately ½ inch in diameter and 2 inches in length, which is placed within the outer tube of the inserter so that a short tuft of the tampon projects from within the tube for a distance of a little over ⅛ inch. This tuft by virtue of slight expansion of the cotton fibers forms a mushroom wedge over the end of the tubing. The removal string is approximately 4¼ inches in length. Insertion is effected by means of pressure on the inner tube which acts as a plunger when the outer tube is inserted in the introitus.

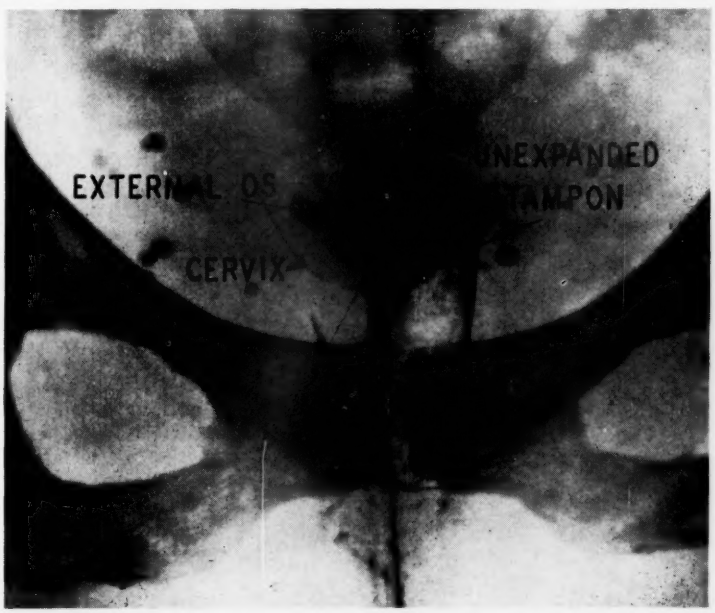

Fig. 11.—Tampon 12, shows tampon in vagina immediately after insertion.

Tampon No. 12—this is a compressed type of tampon made of a 4-inch square of cotton with two lateral edges folded to the center to form a strip 4 inches long and 2 inches wide, with fibers running lengthwise. A chain-lock loop of cord encompasses the middle of this strip before it is folded in half. A double length of cord hangs free from the tampon for a distance of about 3¾ inches. Compression and shaping results in a tampon measuring approximately 1½ inches in length and 9/16 of an inch in diameter with a hollow core extending almost the entire length of the tampon. When fully expanded, the length never exceeds 2 inches which is the length of the folded strip before compression. The inserter consists of an outer tube of kid-glazed paper approximately 3 inches in length and ⅝ of an inch in diameter. The outer tube or casing has a finished edge at its open end which enters the vagina during insertion. The closed end holds the inner tube or plunger in place. The two ends of the plunger are flared outward to prevent dislocation of the two parts during use. The tampon is entirely contained within the inserter, and the strings protrude from the free end of the plunger. The entire unit is individually wrapped in transparent parchment paper.

In this study of tampon No. 1 (the nonexpanding cotton ball type), it was considered inadequate in 3 instances; adequate in 12. None reported discomfort and only one reported a clot. The insertion of this nonexpanding "cotton ball" type of tampon is difficult. Incomplete insertion within the introitus is the usual result, but the softness accounts for the lack of discomfort felt. Contamination is unavoidable.

In the use of tampon No. 2 (fixed length of 2⅛ inches with lateral expansion only): Protection was considered adequate in 14 instances, with one report of leakage after 3 hours. It was reported comfortable in 8 instances, with 7 reports of slight discomfort at the introitus. There were 4 reports of a few small clots, and 11 of no clots. In the use of tampon No. 2, discomfort at the introitus in almost one-half of the cases is caused by the length of the tampon. Insertion is also a problem since contamination of the vagina cannot be avoided, and placement within the introitus cannot be readily accomplished.

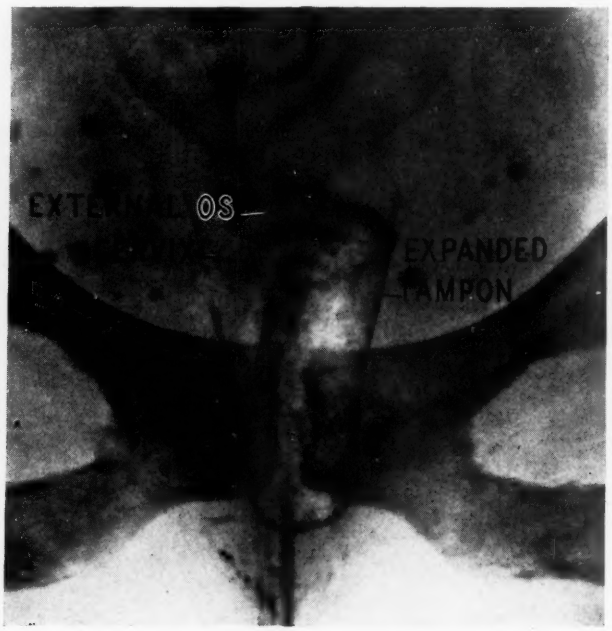

Fig. 12.—Tampon 12, shows tampon 60 minutes after insertion showing expansion.

Study of tampon No. 3 (nonexpanding). Protection was reported adequate in 12 instances, inadequate in 2. The tampon was comfortable in 5 instances, slight discomfort was reported in 6 instances. In 13 instances, there were no clots, in 2 a few small ones. In the use of tampon No. 3 discomfort at the introitus is caused by the length of the tampon. Insertion without contamination is difficult, and placement within the introitus is not readily accomplished.

Study of tampon No. 4 (nonexpanding). Protection was reported adequate in 11 instances; inadequate in 4. It was comfortable in 4 instances, but there were 4 complaints of discomfort at the introitus, 2 complaints of "burning," one of pain due to the length of the tampon, and one of a feeling of "heaviness." Discomfort at the introitus and the other complaints in the use of tampon No. 4 indicate that this tampon

TABLE I. PHYSICAL EXAMINATION OF WOMEN USED IN STUDY OF TAMPONS

CASE	EXTERNAL GENITALIA	VAGINA (DEPTH)	CERVIX	UTERUS	ADNEXA
1	Normal	3 inches	Infantile	Infantile anterior	Slight tenderness
2	Normal	4 inches	Erosion Small	Small anterior	Negative
3	Normal	4 inches Narrow	Nabothian cyst	Small anterior	Negative
4	Relaxed	4½ inches Rectocele Cystocele	Slightly enlarged	Enlarged anterior Fibrotic Tender	Negative
5	Relaxed	4½ inches Rectocele Cystocele	Prolapsed	Small 3-inch retroversion	Thickening in left fornix
6	Normal	3½ to 4 inches	Infantile	3-inch retroversion	Mass—left fornix
7	Normal	3½ inches	Normal	3-inch retroversion	Mass—left fornix
8	Normal	4½ inches	Soft	Slightly enlarged Tender	Thickening and tenderness in fornices
9	Normal	4 inches	Normal	Small anterior	Negative
10	Normal	2½ inches	Erosion Infantile	Small anterior Small fibroid	Negative
11	Normal	3½ inches	Infantile	Infantile anterior	Negative
12	Normal	4½ inches	Normal Lacerated	Small anterior	Negative
13	Normal	3½ to 4 inches	Small	Small 3-inch retroversion	Negative
14	Relaxed	4 inches	Normal Lacerated	Small 3-inch retroversion	Thickening in left fornix
15	Normal	4½ inches	Normal	Small	Negative
16	Normal	3 inches	Elongated	Small 3-inch retroversion Nontender	Slight thickening and tenderness in fornices
17	Normal	3½ inches	Erosion (healing)	Small 3-inch retroversion	Negative
18	Normal	3½ inches Narrow	Slight erosion	Small anterior	Negative
19	Relaxed Gaping	4½ inches	Lacerated Erosion	Small anterior Retrocessed Small fibroid	Negative

TABLE I—CONT'D

CASE	EXTERNAL GENITALIA	VAGINA (DEPTH)	CERVIX	UTERUS	ADNEXA
20	Relaxed Gaping	4 inches	Lacerated	Slightly enlarged Fibrotic	Right and left ovaries prolapsed
	This woman has undergone operation for menorrhagia and metrorrhagia which she complained of, before being used in tampon series.				
21	Normal	4 inches	Normal	Small anterior	Negative
22	Normal	3½ inches	Erosion	Small	Negative
23	Gaping Relaxed Slight irritation Frothy discharge	4 inches Cystocele	Lacerated	Small anterior	Negative
24	Normal	4 inches Rectocele	Lacerated Eroded Bleeding from external os	Small anterior	Tenderness in fornices
25	Normal	4 inches	Small	Slightly enlarged 1-inch retroversion Drawn to left	Negative

is too long for the average woman. Insertion by the fingers results in contamination, and placement within the introitus is difficult and not always completed. In 14 instances, no clot was found, one report mentioned a few small clots.

Study of tampon No. 7 (2-way expansion). Protection was reported adequate in 7 instances; 8 reported leakage. No discomfort in 9 instances, but 6 complaints of discomfort at the introitus or a "heavy" feeling. Proper placement of tampon No. 7 without contamination is aided by the use of an inserter. Placement within the introitus accounts for the lower incidents of discomfort, although the tampon is too long for the average vaginal tract. It displaces the cervix or expands outwardly to cause discomfort. No clots in 13 instances; one with a few small ones.

Study of tampon No. 12 (2-way expansion). Adequate protection reported 11 times; one report of leakage and 3 of slight leakage. Thirteen reports of "comfortable"; 2 of slight discomfort. Eleven reports of no clot; 3 of a few small clots. The use of an inserter with a shorter tampon reduces the incidents of discomfort if proper placement is accomplished. Contamination is avoided. In this and in all the previous studies, the absence of clots on the tampons in the greater number of cases is significant, since it proves that menstrual blood is not dammed back by the presence of a tampon within the vagina.

PART II

Roentgenogram visualization of the position and action of catamenial tampons within the vaginal tract was undertaken. Difficulty was encountered until a radiopaque substance could be prepared that would

mix well with menstrual blood in the vagina. It was considered desirable to develop a technique whereby the tampons could be inserted and observed.

The cervix and the vagina were well exposed by means of an O'Sullivan-O'Connor vaginal speculum, and the walls thoroughly swabbed with a preparation compounded in the following manner: Ten grams of sodium tetraiodophenolphthalein were dissolved in sterile water to make a saturated solution, to which sufficient powdered gum acacia (approximately 2 to 3 grams) was added to thicken the solution. This preparation was allowed to stand one hour before use, with frequent thorough stirrings. The use of this preparation resulted in a soft outline of the vagina and cervix. The tampons were dusted with dry powdered barium sulfate before insertion, resulting in a sharper outline. Exposures were made after preparation of the vaginal tract, and again after insertion of the tampons. In the case of compressed tampons, exposures were made again after an interval to allow expansion to take place. The tampons were inserted by the women themselves.

Summary

1. A study of 6 commercially manufactured tampons used for the control of the menstrual flow in women was conducted on a group of 25 women of varying ages and pelvic types.

2. Five of the 25 women subsequently desired childbearing and succeeded, indicating that the use of tampons does not prevent conception.

3. Nine of the 25 women had used tampons at some time previous to this study indicating a fairly widespread acquaintance with the use of tampons as a method of controlling the catamenial flow.

4. Description of the amount of flow by a patient is not always consistent with the number of pads used, indicating that adequate protection can be judged only by correlating the length of complete protection with definite amount of menstrual flow, which can be determined only by weight.

5. Seven of the 25 women had cervical erosions, but only 2 of the 7 had used tampons previously. Of the 2 who had used tampons previously, one had a lacerated cervix resulting from childbirth, and the other had an erosion which is commonly classified as a congenital erosion of the cervix.

A shorter tampon is to be preferred, since its use is least likely to cause pressure against the cervix.

6. Four of the 6 tampons were inserted manually by the women, and 2 were inserted by the use of individual inserters. The use of an inserter permits proper placement of the tampon within the vaginal tract without contamination by the fingers.

7. Three of the 6 tampons are of the nonexpanding type with a fixed length. Tampon No. 1 is the shortest being only 1⅜ inches. Tampon

No. 3 and tampon No. 4 are both over 2 inches in length. Clinical findings favor the shorter tampon.

8. The remaining 3 tampons are of the expanding type. Tampon No. 2 has a fixed length of 2⅛ inches, and expands only laterally. The other two expand both laterally and lengthwise. Tampon No. 7 has a fixed length of 4 inches before compression, and the other tampon No. 12, has a fixed length of 2 inches before compression.

9. Roentgenogram visualization of the position in action of catamenial tampons indicates that tampons approximately 2 inches in length are least likely to deflect the cervix, in the average woman. Tampons with a rounded base are readily removed.

The study taken as a whole leads to the conclusion that catamenial tampons can be used by the average woman to control an average catamenial flow with safety, comfort, and complete protection, provided that a short tampon is properly placed well within the introitus.

The author wishes to express her appreciation to Dr. Benjamin P. Watson, professor of Obstetrics and Gynecology, Columbia University for his interest in and supervision of this study.

VAGINITIS TREATED WITH AN ANTISEPTIC BUFFERED ACID JELLY*

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THAT leucorrhea remains as a present-day problem is borne out by Polak's statement that 85 per cent of women, married or single, have infected cervices.[1] Many publications report figures indicating that *Trichomonas vaginalis* infections are present in 25 to 33 per cent of women.

Recently, several papers have appeared in the literature regarding the effective use of buffered acid jellies in the treatment of various vaginal infections. The change to present-day conceptions of vaginal physiology may be summarized by the editor's statement in the Yearbook of Obstetrics and Gynecology, 1943,[2] "During the past few years we have come to recognize the importance of the pH of the vagina. Nearly all vaginal infections can be more readily cured by maintaining a low pH medium than by any other method of treatment. Regardless of the drugs used, the important consideration is the pH."

In an extensive and excellent study of vaginal infections, Rakoff and Casper,[3] utilizing an original x-ray technique, reported interesting results following the use of different products. It was concluded that water-dispersible jellies, adjusted to the proper acidity (pH 4.0) are preferable as bases for solutions, suspensions, antiseptics, fungicides, sulfonamides and estrogens. Conversely, capsules and tablets were not satisfactory. A practical point is that the medication may be continued by the patient at home.

Chrisman,[4] using a buffered acid jelly reported excellent clinical response in 100 of 129 cases within seven weeks. These included nonspecific vaginitis, cervicitis, trichomonas vaginitis, cervical erosions, and vulvar and urethral irritations. Definite relief and improvement occurred in one to two weeks. An interesting observation was that the average pH of the posterior fornix prior to therapy was 7.8 and often as high as 8.0 or 9.0. Following administration of buffered acid jelly, within six weeks, the midvaginal pH was 4.0 to 5.0 and the pH of the posterior fornix 4.5 to 5.5.

From 1936 to 1940, Roblee[5] reported definite clinical response with the use of anhydrous lactose to create a vaginal environment of pH 4.5.

Roblee,[6] 1943, combined a buffered acid jelly (pH 4.0 to 4.5) with a sulfonamide and obtained satisfactory results in 112 cases of conization of the cervix and 71 cases of vaginitis. He concluded that buffered acid jellies are of value in the management of cervicitis, vaginitis (especially trichomonas), and monilia infections.

*Caprokol Jelly, which consists of hexylresorcinol 1:1,000 in a buffered base titrated to a pH of 2.0, was generously supplied for this study by Dr. Earl L. Burbidge, of the Medical Research Division of Sharp & Dohme, Philadelphia, Pa.

Allen and Baum,[7] 1942, reported 282 patients treated by means of vaginal instillations of acid buffered water-soluble jellies. The pH as well as medicaments were varied. They found that nitrazine paper was sufficiently accurate to measure pH, the results having checked within a range of 0.5 when compared with the Beckman potentiometer. The authors conclude in part, that a buffered acid jelly is an effective and acceptable method for the treatment of vaginitis, providing symptomatic relief (84 per cent of patients) and causing apparent cures in monilia and nonspecific infections.

In 1940, Bland and Rakoff,[8] used a buffered acid jelly at pH 2.5 to 4.6 and found it extremely useful in the treatment of nonspecific infections of the vagina, cervicitis, endocervicitis, traumatic injuries and in the alteration of the vaginal flora.

Karnaky,[9] in an extensive review study, found that the most important factor in treating trichomonas vaginitis was the pH, and that to be effective, solutions, tablets, powders or jellies should be pH 5.0 or lower.

Vaginal physiology is characterized by cyclic changes. In childhood and after the menopause, estrogenic production is at a low level, the glycogen content of the vaginal epithelial cells is decreased or absent, and Döderlein's bacilli are usually not present. These factors produce an alkaline environment in the vaginal tract which is conducive to the growth of pathogenic organisms and organisms which are not normally a part of the vaginal flora (*B. coli, staphylococci, streptococci, trichomonas, monilia,* etc.). The normal acid reaction is determined by the glycogen content of the vaginal cells, which in turn, is dependent on the estrogenic level present. Döderlein's bacilli, which are acid forming organisms, utilize the available glycogen and maintain a pH of between 4.0 to 5.0. This is an unsuitable environment for pathogenic organisms, the majority of which require an alkaline medium for growth and reproduction.

The present study was instituted with the object in mind to provide replacement therapy locally in an attempt to cause a rapid return to normal and physiologic conditions within the vagina.

In 1931, Greenhill[10] reported the effective use of hexylresorcinol solution in combating *Trichomonas vaginalis* infections. Moore,[11] in 1941, reported the use of a water-soluble jelly containing hexylresorcinol in the treatment of trichomoniasis. The solution was found to be efficacious, but uniformly excellent results (87 per cent) were obtained in Moore's study. The jelly also used in Greenhill's study of 145 patients, is buffered and maintains a pH of 2.0. In addition, hexylresorcinol 1:1,000 provides an effective germicide with a low surface tension which is of definite value in reaching the entire surface of the vagina, and also adds local anesthetic and antipruritic activity. Other similar jellies do not provide as low a pH as the preparation used in this investigation and those referred to above.

The following types of cases were treated with this preparation:

Trichomonas vaginitis	13
Monilia vaginitis	3
Pruritic vulva	5
Nonspecific vaginitis	10
Postpartum cervicitis	14
Postpartum vaginitis, without appreciable cervicitis	12
Antepartum vaginitis, of which 10 showed trichomonas	36
Postpartum vaginitis with erosion	20
Tender episiotomy scar with vaginal hyperemia	4
Senile vaginitis	2
Vaginitis in nullipara with dysmenorrhea	1
Vaginal surgery with postoperative discharge	3
Venereal warts in obstetric patients	5
Hypo-estrinism	4
Vaginitis—nonspecific treated with Caprokol Jelly and Stilbestrol	12
Acute vulvitis	1

At the time of the first examination, pH determinations were made using pHydrion paper.* The container for this paper shows color indicators for a pH ranging from 1 to 11. This paper, when tested with the hexylresorcinol jelly showed a pH of approximately 1.0. Specimens for estimations of the pH were taken from both the cervix and vaginal wall with a cotton applicator, or with a bulb on a glass rod used for aspirating vaginal secretions.

Vaginal smears were made and stained in representative types of cases. The appearance of the cells and the pH of the vaginal secretions depends upon the menstrual cycle and the amount of inflammatory reaction present.

The patient is provided with specific instructions regarding the use of this preparation. She is advised either to boil the glass applicator, or to cleanse it with rubbing alcohol before inserting into the vagina. The jelly is instilled twice daily, morning and evening, during the acute stage of an infection. One application consists of approximately 5 c.c. of the preparation. Should the vaginal discharge be extensive, a perineal pad may be used. Rapid improvement occurs, within one to two weeks and the instillation of the jelly can be reduced to one application daily. A boric acid douche is advised before the patient reports for examination and follow-up study.

The earliest the jelly has been given to pregnant patients was in the second month and the latest, the eighth month. The jelly may be used without danger of introducing infection which might occur when an irrigation or douche is employed.

Patients with pelvic pathology other than cervicitis and vaginitis were excluded from this study. Hexylresorcinol jelly has been utilized in a wide variety of conditions. Numerous reports are available including various types of medication used in the treatment of vaginal infections. In postpartum cervicitis, it was found that the medicated jelly with a pH of 2.0 controlled the infection promptly and as efficiently as douches, tampons or powders. In four of fourteen patients, it was necessary to

*Manufactured by the Central Scientific Co.

coagulate the cervix. In twenty cases of postpartum vaginitis with cervical erosion at the six weeks' examination period, all but one had a complete reversal of the pathologic condition after a course of treatment with the jelly.

It has been observed that in comparison with other methods used to correct the majority of vaginal infections, the preparation used in this study has been the most effective agent yet available in healing erosions and allied infections. It must be noted, however, that a certain percentage of patients has presented recurrences of infections and during the wartime shifting of population, it has been difficult to follow most patients long enough to be certain of permanent results. Ten per cent of patients found to have acquired a *Trichomonas vaginalis* infection have shown recurrence or reinfection, and have returned for further therapy with the jelly.

Additional evidence that this jelly is a valuable addition to our armamentarium is the fact, that patients who have used various douches, powders and other agents have stated that nothing else has given as rapid relief, or is as easy to use as is the hexylresorcinol preparation.

Postpartum vaginal discharge appears to occur more frequently in nervous individuals. Our findings in these cases show a hyperemic and tender mucosa, excessive cervical secretions and usually an alkaline pH.

The results indicate that the medicated jelly employed throughout this investigation is probably most useful during the antepartum and postpartum period. As pregnancy progresses, there is a marked increase in alkaline cervical secretions. Immediately post partum for a few weeks, this is also true. It requires approximately six weeks following delivery before the vagina acquires an acid reaction and returns to the normal physiologic condition. The use of this preparation in the antepartum and postpartum periods is of definite aid in counteracting and controlling the infections which are prone to develop as the vaginal pH increases.

No cases of toxicity or reaction to the jelly were encountered.

Conclusions

1. A series of 145 patients presenting a variety of infections has been studied.

2. "Caprokol" Jelly is a definite aid in the treatment and control of these infections.

3. Normal vaginal physiology is more easily maintained and pathologic conditions reversed.

4. A buffered acid jelly with a pH in the range of 2.0 or less and possessing antiseptic, mildly analgesic and antipruritic properties offers definite advantages in the treatment and control of vaginal infections.

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TRUE KNOTS OF THE UMBILICAL CORD

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TRUE knots of the umbilical cord are not infrequent and are occasionally of a complicated nature. They are usually harmless, since they are rarely pulled tight enough in utero to obliterate completely the lumen of the vessels, or to cause the death of the fetus. They usually result from the active movement of the child. According to von Winckel, two conditions are necessary for their formation: a cord which in length exceeds twice the distance from the umbilicus to the vertex, and a small fetus or a large quantity of liquor amnii, in order to ensure mobility of the former. No doubt in many cases the knot remains open until labor begins, when the tension imparted to the cord by the descent of the fetus closes it. When the knot has been tightened during pregnancy, distortion of the cord will persist even after it has been untied, owing to the effect of the continued pressure on Wharton's jelly, while if it has formed only during delivery it can easily be straightened out. Although it is possible for the knot to become so tightly drawn as to cause a partial or complete obstruction of the cord circulation, this occurs very rarely. False knots, due to twisting or dilatation of the vessels or accumulations of Wharton's jelly, are of fairly common occurrence, and are readily distinguishable from true knots.

Baudelocque found that in some cases when two or even three knots were present, the fetus was alive and normal. Gardien stated that when the umbilical cord is very long it may become entwined around the child's neck and may even form knots which, however, can never tighten themselves during pregnancy sufficiently to cause the death of the fetus or interference with its growth. Chantreuil, on the other hand, thinks that they may be a cause of intrauterine death and that, even though born alive, the child may be thin and poorly nourished. It is commonly believed that only during labor do knots draw tightly enough to cause fetal death.

Complete absence of movements following extreme fetal activity is significant and is sufficient for a diagnosis when no other reason for this condition can be found. It is no doubt due to the gradual asphyxiation of the fetus from tightening of a knot previously formed.

Tardieu (quoted by Browne) made a knot in an umbilical cord, and after pulling it as tightly as possible pumped fluid into the cord. He found that the fluid would always pass through the knot, which partially untied itself when the vessel in front of it became swollen enough to exert pressure on the cord. He came to the conclusion that the fetus

could in every instance exert a degree of pressure sufficient to maintain the fetal circulation. The pulsations of the cord, by incessant repetition of the shock of pulsation, favor the loosening of the knots. Browne went further with the same sort of experimentation. By applying different weights and pressures to the knotted cord, he showed that under certain conditions more pressure was required to force the fluid through the knot and that this pressure was greater than the fetal heart could exert. He concluded, therefore, that in some cases a knot could interfere with and even completely obstruct cord circulation. If the knot is tightened only during labor, the death of the fetus in utero is probably to be attributed to some other cause.

During labor a true knot may result from the passing of the fetus through a loop of the umbilical cord spread out in the lower uterine segment; it may form as a result of fetal movements; or it may be a possible complication of version. The formation of a knot leads to shortening of the cord, and the knot becomes tightened by the weight or movement of the fetus. This is exaggerated if, in addition, the cord is wound around the body, neck or limbs. In most cases in which the death of the fetus is attributed to a knot in the cord, we find the cord wound once or twice around the neck or body, or under the axilla.

According to Chantreuil, the formation of knots is most likely to occur between the ninth and twelfth week when the fetus is small and the movements free owing to the relatively large amount of liquor amnii. Hyrtl believes that the time of formation of the knot may be in some degree indicated by its location: thus, if it is close to the navel it was probably formed at an early period of pregnancy. Chantreuil points out, however, that owing to the slippery surface of the cord and the slackness of the knot immediately after its formation, it might slide in either direction.

An interesting case of knotting of the cord without injury to the child is reported by Fleming. A woman, 28 years of age, was delivered at full term of a large healthy boy. The cord contained two knots, one a figure-of-eight located about one foot from the placental end, the other a single knot at about the same distance from the umbilical end. The cord was 4 feet long, and both knots were loosely tied. Fleming had observed single knots in the cord in previous cases, but never two knots in the same cord.

The separate cords of twins provide excellent opportunities for unusual twisting, interlacing, and knotting, particularly when the two fetuses are encased in one amnion without a dividing septum.

Case Reports

Seven original cases are herewith briefly described, followed by a tabulation of 32 cases from the literature, supplementing the table published by Browne.

CASE 1.—Primipara, aged 28. Pregnancy normal until 48 hours before onset of labor, when unusually strong active fetal movements were felt (as though the baby had turned completely over), followed by a complete cessation of movements. Spontaneous labor and delivery of a macerated fetus (38 weeks), weighing 6 pounds, 9 ounces, and 20 inches in length. The cord was 60 cm. in length, with a true knot tightly drawn at about the middle. The vessels proximal to the knot were completely collapsed. There was a small partial separation of the placenta, otherwise condition was normal. Wassermann test was negative.

CASE 2.—Primipara, aged 22. After a normal pregnancy, she was delivered normally of a living premature child, weighing 4 pounds, 14 ounces, and 18 inches in length. The cord was 58 cm. long and contained a true knot, not tightly drawn, about 28 cm. from the placenta.

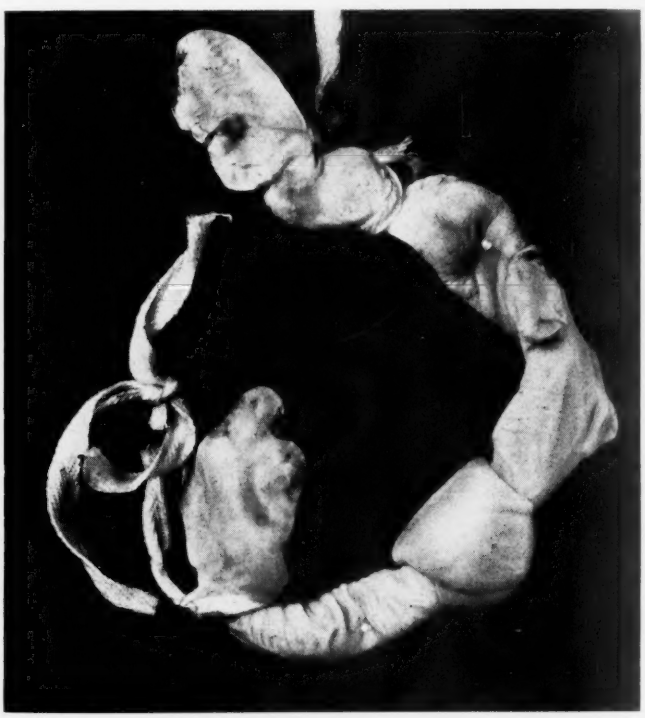

Fig. 1.—Showing one true knot tightly drawn, delivered of a dead baby (macerated).

The cord was around the right leg and right arm. The placenta was normal and the Wassermann test negative. The baby's progress was satisfactory.

CASE 3.—Para iii, aged 37. Normal pregnancy and normal delivery after four hours of labor of a 9-pound living male child. The cord was 56 cm. in length and contained two true knots, 7.5 cm. apart; the first knot 24.5 cm. from the placenta, and the second 31.5 cm. from the placenta. The placenta was normal and the Wassermann test negative. There had been no unusual symptoms prior to labor.

CASE 4.—Primipara, aged 28. Normal pregnancy, with no unusual symptoms. Labor, lasting 13½ hours, was followed by delivery of a

living male child weighing 7 pounds, 3 ounces. The cord was 66 cm. long and had two true knots; the first 30.5 cm. from the placenta, the second 41 cm. from the placenta. The placenta was normal, the Wassermann test negative. (Fig. 2.)

CASE 5.—Primipara, aged 36. Normal pregnancy, followed by normal delivery, lasting 5 hours, of a living male child. The cord was 59 cm. in length, with one true knot, 32 cm. from the umbilicus. The placenta was normal, the Wassermann test negative.

Fig. 2.—Showing two true knots, delivered of a living baby.

CASE 6.—Para ii, aged 23. Normal pregnancy; no symptoms. Normal delivery of a living female child, weighing 7 pounds, 12½ ounces, and 19 inches in length. Labor lasted 2½ hours. The cord was 61 cm. in length, with one true knot, 15 cm. from the placenta. The placenta was normal, the Wassermann test negative.

CASE 7.—Para ii, aged 38. Pregnancy was normal, but the patient noticed a cessation of fetal movements 80 hours before the onset of labor. No unusual activity had preceded the cessation. After labor lasting 1 hour and 10 minutes, normal delivery of a male macerated fetus weighing 7 pounds, 9 ounces, 20 inches in length. The cord was 74 cm. in length and contained one true knot, tightly drawn, 49.5 cm. from the umbilicus. The placenta was normal, the Wassermann test negative. (Fig. 1.)

TABLE I

OBSERVER AND DATE	AGE	PARA	ALLEGED CAUSE	SYMPTOMS	LENGTH OF CORD	NO. OF KNOTS	SITUATION OF KNOT	VARIETY OF KNOT	PRESENTATION	REMARKS
Fleming 1924	28	7	--------	----------	48 in.	2	First, 1 ft. from placental end; second, 1 ft. from umbilical end	First figure of eight; second single	--------	----------
Atwood 1932	34	3	--------	Pain 10 days prior to admission; unusual fetal activity	--------	1	Middle of cord	Sailor	--------	----------
Atwood 1932	42	--	--------	----------	--------	--	----------	Cords intricately knotted	Breech	Mono-amniotic twins (male)
Ceicys 1936	23	1	--------	----------	--------	--	Close to umbilicus	--------	--------	----------
Ceicys 1936	32	1	--------	----------	--------	--	----------	--------	--------	Mono-amniotic twin 6 months; cords knotted together
D'Elia 1938	--	1	--------	----------	90 cm.	1	25 cm. from placenta	Double	Vertex	Forceps; asphyxiated; died shortly after birth
Emmanuel 1930	43	4	--------	----------	First 80.5 cm.; second 94 cm.	1	----------	True	H.H.L.	Second twin died 1 hour before birth; knot drawn tight
Floyd 1934	26	2	--------	----------	--------	1	Near junction of middle and placental thirds	True	Vertex	Heart sounds and movements normal; baby alive and well; knot not tight
Gallucci and Delascio 1941	30	2	--------	----------	--------	1	Middle portion of cord	--------	Vertex	Cesarean section
Itzkin 1929	27	1	Unusual length of cord	Fetal movements ceased 10 days before labor; no F.H. sounds	75 cm.	1	About middle of cord; 36 cm. from umbilicus	Single true knot	--------	Male macerated fetus

Kittler 1928	27	2	Fall; next day abdominal pain	Cessation of fetal movements	45 cm.	1	Looped around the fetus and tied	Double true knot	Vertex	Premature macerated fetus
Litt and Strauss 1935	30	3	--------	Cessation of fetal movements 4 days before labor	--------	Multiple	30 cm. from placenta, entangled and knotted in multiple true knots	True, multiple	1. Breech 2. Vertex	Mono-amniotic twin pregnancy. (1) Anencephalic monster; (2) macerated fetus
Lundgren and Boice 1939	26	1	--------	Cessation of fetal movements 2 days before admission	120 cm.	2	----------	Half-hitch 1 foot apart	Vertex	Macerated; dead about 4 days
Lundgren and Boice 1939	--	--	--------	----------	Normal	1	----------	True tied knot	Vertex	Stillborn
Lundgren and Boice 1939	30	6	--------	Cessation of fetal heart sounds before delivery	65 cm.	2	----------	True	--------	One knot very tight and proximal vessels collapsed
McCormick 1929	31	1	Fall at 7½ months' gestation	----------	--------	1	----------	Loose figure-of-eight	--------	----------
McNally 1938	29	4	--------	Cessation of fetal movements 72 hours before labor	62 cm.	1	17 cm. from child	True	Vertex	Normal delivery; dead male child macerated
Mitchell 1939	29	4	--------	Unusually active fetal movements; ceased next day	82 cm.	1	54 cm. from placenta	True, tightly drawn	--------	Spontaneous delivery of dead macerated child
Montanari 1939	24	2	--------	10 days before delivery violent fetal movements, lasting 1 hour, then cessation	50 cm.	Mult.	Middle of cord	True	--------	Believes knots are formed at early period when fetus is most active toward end of sixth month
Nizza 1933	29	2	Length of cord	----------	70 cm.	Mult.	50 cm. from placenta	True	Cephalic	Delivery at 7 months, twins, both living
Quigley 1935	34	1	Mono-amniotic twin pregnancy	Only one fetal heart heard	--------	Several	----------	True	Vertex	Stillbirths; twin cords inserted marginally 9 cm. apart

TABLE I—CONT'D

OBSERVER AND DATE	AGE	PARA	ALLEGED CAUSE	SYMPTOMS	LENGTH OF CORD	NO. OF KNOTS	SITUATION OF KNOT	VARIETY OF KNOT	PRESENTATION	REMARKS
Trettenero 1928	27	2	--------	----------	101 cm.	1	84 cm. from placenta	True	Vertex	----------
VerHoef 1929	27	1	--------	No fetal movements since first pains	70 cm.	1	20 cm. from placenta	True	--------	Stillbirth; knot tightly drawn
Beard T.C. 1944	--	3	--------	----------	24 in.	1	Not given	True	Vertex	34 weeks. Normal delivery; alive. Spina bifida. Lived 7 days; infection
Coulson 1944	26	1	--------	Fetal distress; much meconium	--------	1	Not given	Glove tight	Vertex	Twice around neck; shocked. Baby made good recovery
Hennessy	28	1	--------	Cessation of fetal movements 48 hours before labor	60 cm.	1	29 cm. from placenta	True	Vertex	Tightly drawn knot. Fetus macerated, 38 weeks
Hennessy	37	3	--------	----------	56 cm.	2	First knot 24.5 cm. from placenta; second knot 31.5 cm. from placenta	True	Vertex	Normal delivery of a 9-pound living male
Hennessy	22	1	--------	----------	56 cm.	1	25 cm. from placenta	True	Vertex	Knot loose around right leg and right arm. Living baby (32 weeks)
Hennessy	28	1	--------	----------	66 cm.	2	First knot 30.5 cm. from placenta; second knot 41 cm. from placenta	True	Vertex	Normal delivery of a living female
Hennessy	36	1	--------	----------	59 cm.	1	32 cm. from placenta	True	Vertex	Normal delivery of a living child.
Hennessy	23	2	--------	----------	61 cm.	1	15 cm. from placenta	True	Vertex	Normal delivery of a living child
Hennessy	38	2	--------	Cessation of fetal movements 80 hours before labor	74 cm.	1	49.5 cm. from umbilicus of fetus	True tight	Vertex	Normal delivery of a macerated male, 7 pounds, 9 ounces, 20 inches

Summary

1. True knots of the umbilical cord are fairly common.

2. They may exist during intrauterine life without endangering the life of the fetus.

3. They sometimes obstruct cord circulation sufficiently to cause death of the fetus.

4. Usually they are of little clinical importance.

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116 EAST 68TH STREET.

CLINICAL SIGNIFICANCE OF STRUMA OVARII

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THERE have been eight cases of struma ovarii recorded in the pathologic files of the Sloane Hospital for Women in the past 20 years. This represents 2.7 per cent of 297 ovarian teratomata of all types which were examined during the same period. In addition to these, several thyroid rests have been observed; the diagnosis of ovarian struma, however, has been confined to those tumors which contain significant quantities of thyroid tissue.

Of the eight cases reported here, seven presented the usual array of clinical symptoms and signs which ordinarily accompany benign ovarian tumors: intermittent abdominal pain, painless pelvic or abdominal masses, and, in one instance, acute abdominal pain due to torsion of the pedicle. In these cases, the presence of thyroid tissue is of pathologic interest only. The cystic tumors were generally multilocular, and three of the seven contained epidermoid elements characteristic of the ordinary dermoid cyst. Microscopically, none of these cases showed evidence of hyperplastic changes in the thyroid tissue. The eighth case, however, presented a symptom complex of an unusual nature, the diagnostic and therapeutic implications of which are deemed significant. This case is therefore presented in detail.

Case Report

Mrs. J. J., aged 53, para viii, gravida viii, presented herself at the Presbyterian Hospital in September, 1943, with the chief complaint of goiter of 35 years' duration. She was admitted to the surgical wards for study shortly thereafter, and in October, readmitted for thyroidectomy.

History: On admission, there were three groups of significant symptoms:

(a) A history of goiter-like swelling in the neck for 35 years. This had been noted after her first pregnancy, and had enlarged thereafter with each pregnancy, and also to a notable degree for the five years prior to admission.

(b) The patient had noted mild exertional dyspnea for approximately two years, and some difficulty in swallowing for several months prior to admission. She had had a relatively uneventful menopause 14 months before entry to the hospital, but since that time had experienced mild palpitation, insomnia, increased perspiration and some nervousness. Mild tremor of the fingers and increasing fatigability had been noted recently.

(c) A progressively enlarging abdominal swelling had been present for 1½ years.

Physical Examination confirmed the presence of thyroid and abdominal masses. The thyroid was enlarged to "football" size. It felt irregularly cystic and lobular. The abdominal mass was irregular, cystic and moderately mobile; it filled the lower abdomen and rose almost to the costal margin on the left. There were no eye signs of thyrotoxicosis. There was a slight tremor, and mild cardiac hyperactivity. Moderate tachycardia was constant. The blood pressure on admission was 150/70.

Laboratory Data: Basal metabolic rates were obtained ranging from +30 per cent on 9/21/43 to +61 per cent on 10/21/43. These were followed by readings of +56 per cent on 11/1/43 and +55 per cent on 11/8/43. Blood cholesterol was 161 mg./% on 10/21/43 and blood iodine 15.1 gamma/% on 10/22/43. This latter observation was made three weeks after cessation of a previous course of iodine therapy and is considered significant.

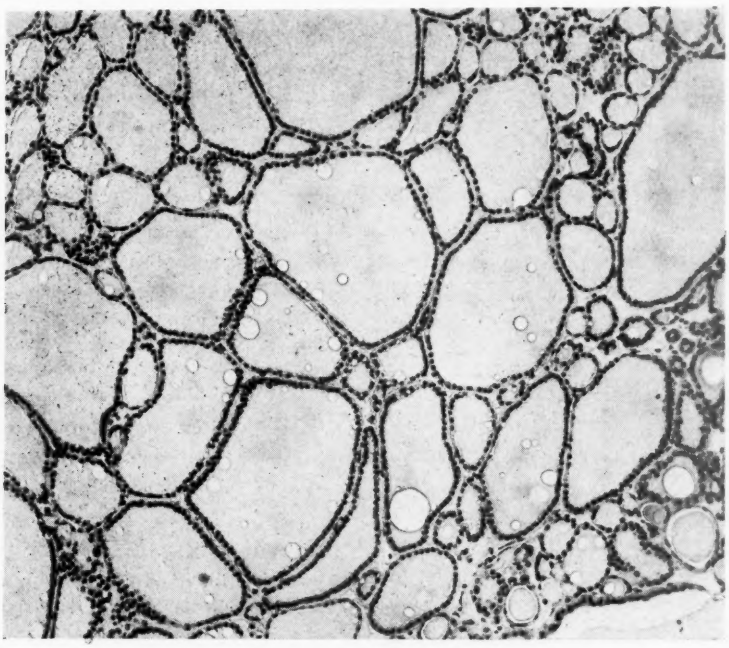

Fig. 1.—The goiter ×150.

Course: On her first admission, the patient was given a course of iodine therapy which consisted of 1 c.c. of Lugol's solution daily for 12 days. This had no perceptible effect on her general status. On readmission, another course of Lugol's solution had a slight ameliorating effect on her pulse and symptoms, but none on the basal metabolic rate.

Since the abdominal tumor was regarded as an ovarian cyst, it was deemed advisable to deal with the thyroid problem first. Therefore, on 11/10/43 a partial thyroidectomy was performed. At operation, the thyroid was represented by a huge irregularly cystic nodular mass which measured approximately 26 cm. in its greatest diameter and weighed 920 Gm. on removal. Microscopic examination revealed acini which varied markedly in size; many were distended by colloid and lined by flattened cuboidal cells; a few smaller acini were lined by higher cuboidal cells. In some of the more solid portions of the gland, focal

collections of lymphocytes were seen. There were occasional areas of degeneration and old hemorrhage throughout. It was the opinion of Dr. V. Kneeland Frantz of the Department of Surgical Pathology of the Presbyterian Hospital, who examined these sections, that the bulk of the tissue was involuted; furthermore, she was not able to correlate the histologic picture with the clinical evidence of toxicity.

The patient made a relatively uneventful recovery from the thyroidectomy. A moderate to mild tachycardia persisted, but its significance was difficult to evaluate because of some anemia. The patient was improved subjectively. Her basal metabolic rate on 11/22/43 was +10 per cent. Throughout her hospital stay, she was kept on iodine therapy.

The patient was discharged home for interval convalescence; she felt fairly well in the interim and was admitted to the Sloane Hospital in January, 1944, for removal of her abdominal tumor. Upon admission, there was mild tachycardia and nervousness; the blood pressure was 170/102. No other significant symptoms or signs of thyrotoxicosis were elicited.

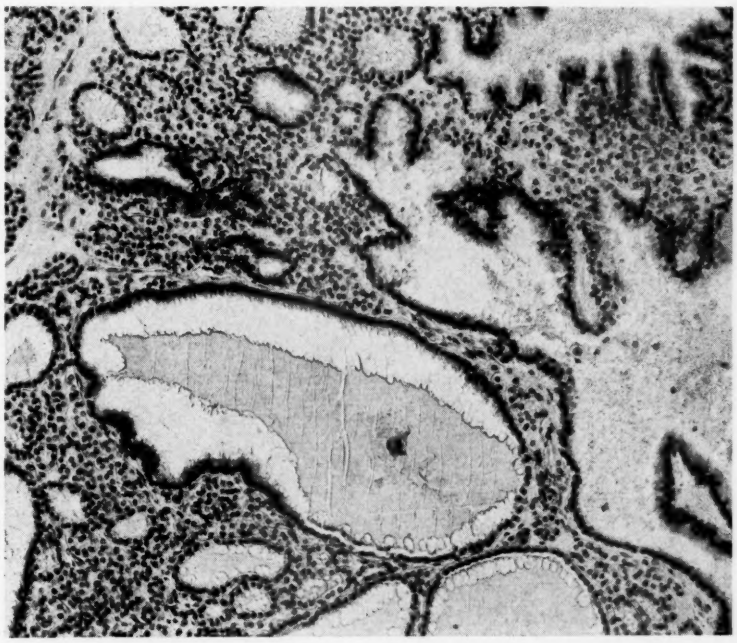

Fig. 2.—The struma ovarii ×150.

At laparotomy on 1/11/44, a large tumor was found arising from the left adnexal region and filling most of the abdominal cavity. The uterus appeared normal; the bowel was adherent to the tumor mass in several areas but the peritoneum was otherwise clear. A supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed.

Pathologic examination revealed the endometrium to be mildly hyperplastic, and the right ovary to be the site of a small serous cystadenoma. The left ovary had been replaced by a huge multilocular tumor mass measuring 23 by 12.5 by 8.5 cm. Approximately three liters of fluid had already been removed from one locule at operation. Some locules were lined by a smooth grayish-tan membrane and contained clear yellow

fluid. About one-third of the total volume of the tumor was occupied by a honeycombed gland-like tissue which resembled thyroid tissue grossly. On microscopic examination, a variable pattern was encountered. Stratified squamous epithelium lined some of the spaces, while numerous locules were lined by a single layer of low columnar epithelium. The thyroid portions of this cystic teratoma also varied. There were some small acini closely arranged with cuboidal epithelium lining them. There were also some larger acini with low papillary infolding and low columnar epithelium. It was the impression of Dr. Frantz that the ovarian struma showed more evidence of hyperplasia and less of involution than the goiter. The possibility that the thyrotoxicosis in this case was directly related to the ovarian struma was suggested. The probability that the struma played some role in this endocrine overactivity seems inescapable.

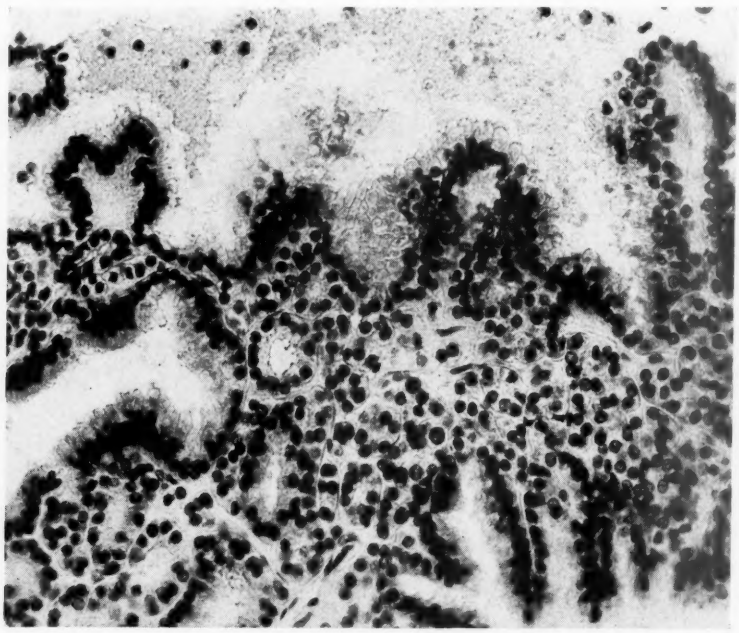

Fig. 3.—The struma ovarii ×300.

The patient made an uneventful recovery from the operation, and has been well and without observed tachycardia or thyrotoxic symptoms since. The basal metabolic rate was noted at −14 per cent on 1/29/44 before discharge from the hospital, and +1 per cent on 2/21/44.

Discussion

The case which we have presented is notable in that a huge struma colli, a large struma ovarii, and evident thyrotoxicosis were coexistent. It is unfortunate that the possibility of ovarian struma was not considered and the preliminary work-up carried out with this in mind. Despite the incomplete data, several points of interest have been derived from the case and from the review of the literature which it has occasioned. The actual role of the ovarian tumor in the production of the

hyperthyroidism is problematical, and no amount of study of the data can produce any conclusive evidence. However, the comparative microscopic findings, the probable mechanical contribution of the huge goiter to the elevated basal metabolic rate, and the persistent tachycardia following thyroidectomy might all be considered as presumptive evidence that the ovarian tumor contributed to the thyrotoxicosis.

That struma ovarii is capable of producing or at least contributing to thyrotoxicosis, is established. It is this ability which distinguishes the ovarian struma among all ovarian neoplasms, and removes it from the category of the simple pathologic curiosity. It should be emphasized that cases of functioning ovarian struma may easily escape diagnosis, either through failure to appreciate mild hyperthyroid symptoms, or through chance avoidance of thyroid tissue in the sectioning of large ovarian teratomata. In 1940, Emge estimated the recorded cases of struma ovarii at 150, of which 5 to 6 per cent were said to have produced thyrotoxicosis.[1] Since this time, some 31 ovarian strumata have been reported;[2-9] of these, eight are said to have been accompanied by thyrotoxicosis. In at least five cases, coincident enlargement of the thyroid was present. In three patients thyrotoxic symptoms were relieved by oophorectomy alone; in two of these, prior subtotal thyroidectomy had failed to arrest the hyperthyroidism.

It is of interest that in most of the cases in which such data are available, the ovarian sections have failed to show the presumed microscopic stigmata of hyperthyroidism, despite amelioration of symptoms by removal of the tumor. It would appear reasonable to consider the ovarian struma as a functioning part of the total thyroid tissue of the body, which may react to iodine lack, to the thyrotropic hormone, or to other stimuli in a manner similar to that of the thyroid gland itself. If this hypothesis is tenable, one might then consider the removal of an ovarian struma as tantamount to subtotal ablation of the thyroid gland. The signal importance of this disease picture is manifested in the case which presents distinct evidence of thyrotoxicosis, plus enlargement of the thyroid gland, plus an ovarian tumor. If the thyroid does not by its very size demand removal, as it did in the case herewith presented, the possibility of a functioning ovarian struma should be considered, and the primary surgical consideration weighed. Two cases of apparently needless thyroidectomy in such a situation are recorded in the recent literature.

Summary

The incidence of struma ovarii among 297 ovarian teratomata of all types removed at the Sloane Hospital for Women during the past 20 years is 2.7 per cent. A case is presented in which thyrotoxicosis, a large struma ovarii, and a huge goiter were coexistent. The recent literature upon struma ovarii is briefly reviewed. The clinical and therapeutic implications of this condition are considered.

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OVARIAN PREGNANCY*

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OVARIAN pregnancy is the rarest type of extrauterine pregnancy. More than 200 cases of ovarian pregnancy have been reported in the literature and all stages of development from the youngest to that of a mature fetus lodged in the ovary, have been found. The number of cases would probably be higher if a complete histologic examination were performed in all cases of hematomas of the ovary, or in those cases where rupture of a follicle or corpus luteum takes place.

According to Spiegelberg the following four requirements were postulated before the diagnosis of a true ovarian pregnancy could be made:

1. The tube on the affected side must be intact.
2. The fetal sac must occupy the position of the ovary.
3. It must be connected with the uterus by the uteroovarian ligament, and
4. Definite ovarian tissue must be found in the sac wall.

It has therefore been claimed that the majority of the cases reported were not true ovarian pregnancies, since all the necessary criteria were not present, and that only about 50 cases could be so classified.

It would seem that some of these requirements are much too rigid, since their presence or absence will depend upon many conditions. If the operation is done some time after the sac wall has ruptured, and the embryo has escaped from the sac, definite changes do take place in the involutional process that may destroy some of the evidence, or the anatomic relations may be distorted by the fetal sac itself; or by the amount of blood in the ovary itself, or clotted blood surrounding the area.

Two etiologically different types of nidation have to be differentiated in the presence of ovarian gravidity—namely, fertilization within the Graafian follicle before the ovum has escaped, or fertilization outside of the ovary. There seems to be no reason why fertilization may not take place in the tube and travel back to become implanted in a recently ruptured ovary, or it may take place outside of the tube or ovary with implantation taking place in the ovary, usually at a point remote from the corpus luteum. In the intrafollicular type, there is a failure in the mechanism of the ovum resulting in fecundation within the follicle.

Of great speculative interest in these cases, as in all types of ectopic pregnancies, is the causal relationship of the presence of endometrial nests in the organs involved. Endometriosis in the ovary is not an uncommon condition, and whether the presence of endometrium is necessary for implantation to take place is unknown. Logically, it would seem that the presence of endometrium is essential, and that implantation cannot take place in its absence.

*Presented at a meeting of The Bronx Gynecological and Obstetrical Society, May 22, 1944.

It is difficult to make a diagnosis of ovarian pregnancy. The symptoms closely resemble those of tubal pregnancy. Rupture may occur later than in the tube, there may be less uterine bleeding, the pelvic pain may not be so acute since there are little if any muscle cramps, and the tumor mass felt on examination may be longer than that of a tubal pregnancy in a corresponding period of pregnancy.

The case to be reported is, we believe, a very good example of the intrafollicular type. The rarity of the condition and the excellence of the specimen justify the presentation of the case as one of ovarian pregnancy.

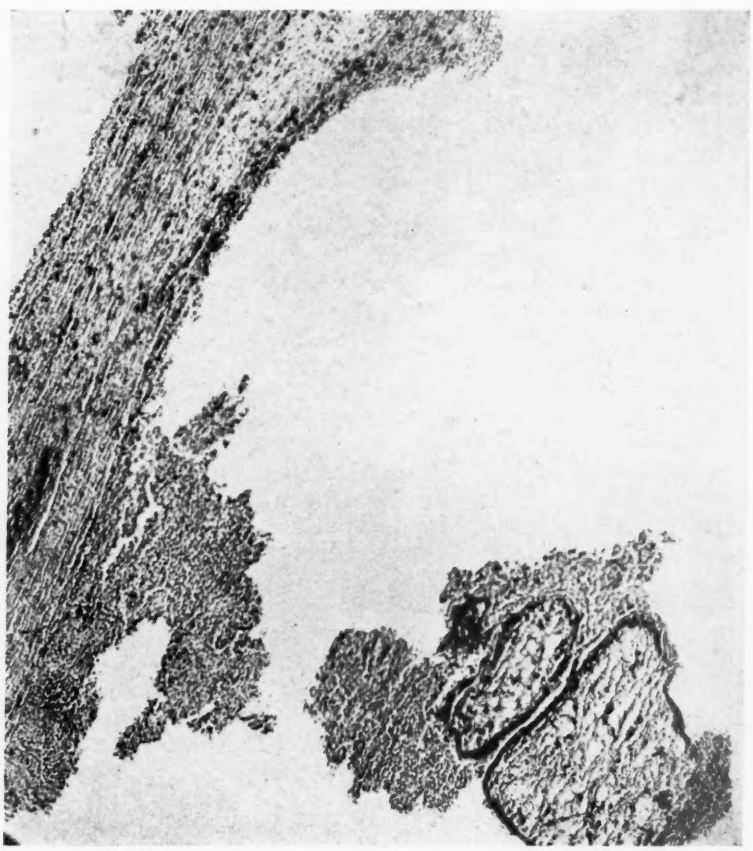

Fig. 1.—(26069.) Microscopic section showing ovarian cyst wall with the presence of adjacent blood clot and chorionic villi. (×300.)

Case Report

HOSPITAL No. 152593.—Mrs. H. N., aged 30, was first seen by the senior author and the following history was obtained. White woman, married, the background of her medical and surgical history was essentially negative. She began to menstruate at the age of 11, regular 28-day intervals, lasting 5 to 6 days. Moderate flow with no pain. She was delivered spontaneously of a living child 6½ years previously.

Her last period was due December 16, which she missed. She began to bleed moderately on December 26, spotting for 6 days. She stopped

for several days and the bleeding returned. With the return of the flow, she began to have lower abdominal pain more or less constant in character and more pronounced on the left side, with frequent urination.

General examination at this time was not relevant. Pelvic examination showed the following: Moderate bloody discharge. The perineum was relaxed, the cervix bilaterally lacerated and pointing in the axis of the vagina. On attempt at motion she complained of pain in the abdomen. The fundus uteri was anterior, slightly enlarged and partially fixed. To the left of the uterus a rounded tumor mass could be palpated easily, about the size of an egg. This was fixed and quite tender. The right adnexa were normal. A diagnosis of left unruptured ectopic pregnancy was made and she was referred to The Bronx Hospital.

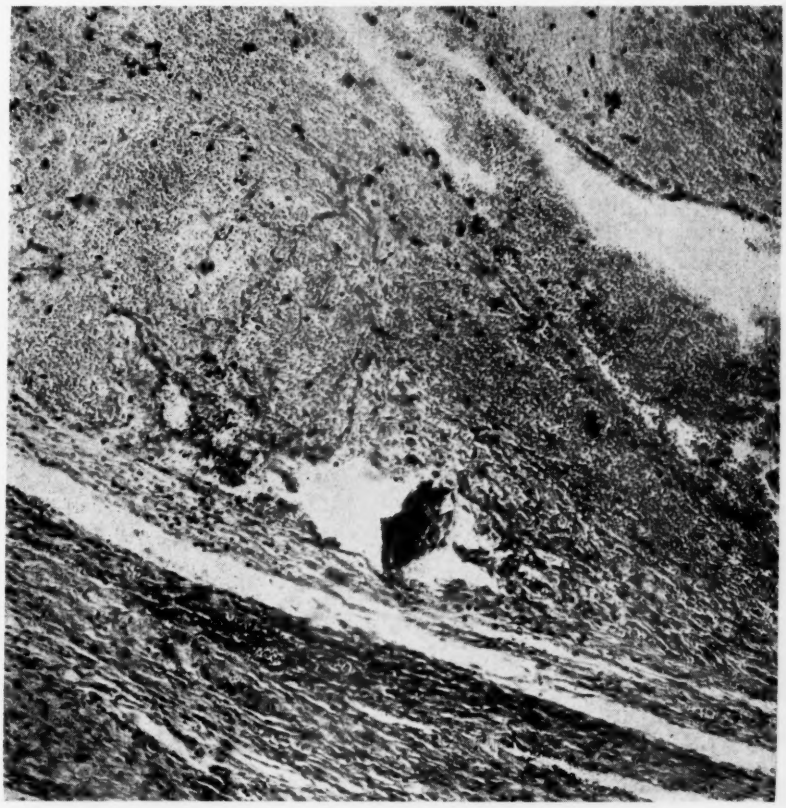

Fig. 2.—(26069.) Microscopic section showing ovarian cyst wall with the adjacent hemorrhage. (×300.)

She was admitted to the hospital on January 10, 1944, and physical examination was as described above. Pulse rate was 72, temperature 99° F., and blood pressure 130/80. The laboratory findings showed a leucocytosis of 11,000 with 61 per cent polymorphonuclear leucocytes, hemoglobin 85 per cent with red cell count of 4,370,000. Urine was negative.

Operation the next day showed the following: In the abdominal cavity, some free blood clots were found in the pelvis and covering the intestines. The left ovary was enlarged to about four times its normal

size. About one-third of the surface of the ovary (anterior) consisted of a craterlike mass filled with organized blood clots. A sharp ridge surrounded this hemorrhagic area. The Fallopian tube was normal in appearance and partly adherent to the ovary. The fundus uteri and right adnexa were found to be normal. A left salpingo-oophorectomy was performed and the abdomen closed. She made an uneventful recovery and was discharged on the twelfth postoperative day.

Pathological Report (No. 26069).—The specimen consists of a tube and ovary. The ovary measures 5 by 4 cm., and is the seat of a 3 cm. in diameter hemorrhagic area filled with friable, villous-like tissue. Its attached tube measures 5 cm., and shows no gross pathology.

Microscopically, sections of the ovary show the presence of blood and chorionic villi adjacent to ovarian stroma (Figs. 1 and 2). Sections of the tube revealed a thickened wall containing dilated blood vessels.

Diagnosis: Ovarian Pregnancy.

We are indebted to Dr. Joseph Felsen, Director of Laboratories, The Bronx Hospital, for the photomicrographs.

900 GRAND CONCOURSE

1840 GRAND CONCOURSE

VAGITUS UTERINUS WITH PROLAPSE OF THE UMBILICAL CORD

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IN OBSTETRIC practice, few incidents are more incredulous than vagitus uterinus, which by definition, is crying in utero. According to Freed,[1] vagitus uterinus was first described by J. B. von Fischer in 1730. However, this rare occurrence apparently was known of before this time for DeLee[2] wrote that Mohammed and St. Bartholomew made themselves heard while in the uterus, but he added that these were probably fables.

Kitzmiller and Mitchell[3] cited three conditions which must be present in order for crying in utero to become evident, namely: (1) the membranes must have ruptured; (2) there is usually some operative manipulation to stimulate the infant; (3) there must be entrance of air into the uterus. They added that points (1) and (3) are generally accepted, but that the second point is in question, that is, whether this stimulation to the infant is central asphyxia, or merely a cutaneous stimulation.

In practically all reported cases, this phenomenon follows some manipulation as application of forceps, version or simple vaginal exploration. Freed observed vagitus uterinus following introduction of his hand into the vagina, as did Morton.[4] In the latter's case, a version was done but the child died. In Flatau's classical case, reviewed by Freed, crying was heard as often as the prolapsed umbilical cord was compressed by the fingers. The explanation offered was that pressure on the umbilical cord would increase the carbon dioxide content of fetal blood and stimulate respiration.

It has been suggested that vagitus uterinus is a sign of fetal distress. Frazier[5] said that his case afforded an exception to this generalization in that the mother, in gestation 31 weeks, was admitted for antepartum hemorrhage. The baby cried for forty minutes, and was delivered precipitately thirty hours later, dying of prematurity and intracranial damage, the latter being due to precipitation.

Clouston[6] noted vagitus uterinus in a patient with brow presentation which he converted into a mento-anterior face presentation and successfully delivered.

In a mother 38 weeks pregnant, with a pelvis suggestive of disproportion, Field[7] ruptured the membranes with a catheter and air was heard being sucked into the uterus through the lumen of the catheter; the infant cried. Fifty-four hours later, the mother delivered a normal child which lived. With delivery of the placenta, a gush of air came from the vagina.

Several cases of vagitus uterinus have been reported in connection with "high forceps." Brodhead[8] had one case and Pease[9] three. High forceps delivery was attempted unsuccessfully in a case recorded by Harrison,[10] and the patient was subsequently delivered of a living 10-pound infant by cesarean section.

Babies who cry in utero have been delivered alive several days after the occurrence. Rucker[11] reported two cases and concluded that the fetal mortality in cases of vagitus uterinus, while not excessive, seems to be due largely to efforts to save the baby from asphyxia by rapid delivery.

If a baby cries in utero, will it drown? Peters[12] said that theoretically, intrauterine crying would entail the danger of the baby drowning in the amniotic fluid, but in practice, this apparently has rarely, if ever, occurred.

Ryder[13] stated that his own brought the total number of authentic cases to 123. It is the purpose of this report to raise that total by one.

Case Report

On January 28, 1944, Mrs. J. L., a 29-year-old para vii, gravida viii, was admitted in active labor with strong pains. Last menses began April 16, 1943, and lasted six to seven days, and she claimed that fetal movements were first felt during the sixth month of gestation.

Twenty-five minutes after admission, the membranes became visible and she was moved to the delivery room. As she was placed on the delivery table, a membrane-covered mass protruded from the vagina. The membranes ruptured spontaneously, and a loop of umbilical cord about 30 cm. in length was found prolapsed. Shortly thereafter, the infant was heard crying loudly enough to be heard by all in the room. The mother, thinking that the baby had been delivered, asked, "Is it a boy or girl?" To her amazement, she was informed that the child had not been born. At the time, fetal heart tones were 100 per minute but were still strong.

Vaginal examination revealed the cervix dilated 6 to 7 cm., cephalic presentation, with the umbilical cord compressed between the fetal head and the superior rim of the cervix. An unsuccessful attempt was made to replace the loop of cord, and it was decided to deliver by version and breech extraction.

Two fingers were inserted as a bridge over the strangulated umbilical cord, and the cervix allowed to dilate. The fetal heart tones were now reduced to 90 per minute and were somewhat irregular. Immediately before delivery, the fetal heart tones were not heard, but it was deemed advisable to continue with the procedure, with the hope of resuscitating the child.

Without unusual difficulty, a female stillborn which weighed 6 pounds, 2 ounces was delivered by combined podalic version and breech extraction. To prevent infection, the mother was given an intrauterine douche with $KMnO_4$-H_2SO_4 solution.

The mother had a temperature of 101.2° F. six hours post partum, but it subsided the same day. The puerperium was otherwise uneventful. The patient signed a release and was discharged on the ninth postpartum day.

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AN ANTEPARTUM STUDY OF FETAL POLARITY AND ROTATION*

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VOLUMINOUS statistics on the frequency of fetal presentations and positions in a large series of cases have been reported in the past and are available in obstetric texts. Most observers have agreed that vertex presentations occur with 95 to 96 per cent regularity, breech presentations with 3 per cent frequency, and face and transverse making up the total. Since the diagnosis of presentation and position depends upon *the time that the diagnosis is made,* much of the labor spent in compiling such statistics was wasted since no standard timing measures were used. Moreover, in most of the earlier studies discrepancies must have occurred frequently since the diagnosis of presentation was made solely on a basis of physical examination without the aid of x-rays.

With the advent of modern roentgenology and the concurrent simplification of radiologic apparatus and technique, much more accurate obstetric diagnoses are being made, and a better foundation of intrauterine physiologic activity of the fetus is being evolved.

While most obstetricians still consider breech presentations eutocia (notwithstanding the trebled fetal mortality, and the greater maternal morbidity from sepsis and lacerations resulting from such deliveries in the hands of the general practitioner who still does most of the general obstetrics), this author believes with DeLee and others that breech presentations should be considered dystocia.

In this respect, exact information relative to such errors in fetal polarity, and the resulting natural and scientific efforts of accommodation and adjustment by rotation and version are of great value. Accordingly, a radiologic antepartum study of fetal polarity from the time when the fetal parts first become visible until just before delivery was considered desirable. This study could only be of value if each individual pregnancy was carefully studied and followed and the progress recorded. The utilization of a pregnancy series of such a magnitude as to become unwieldy and render roentgen observations sporadic and haphazard was at once dismissed in favor of a more carefully controlled smaller group of cases.

Procedure

One hundred unselected primiparous women were studied by ordinary palpatory methods and by x-ray visualization from early pregnancy until term. X-rays of the fetus were taken as early as

*This study was completed before entering the United States Public Health Service. The opinions and assertions contained herein are the private ones of the writer, and are not construed as official, or reflecting the views of the U. S. Public Health Service.

radiopaque shadows could be detected and at regular intervals during the gestation. Plates were exposed at about the fifth month of pregnancy (eighteenth to twenty-second week), the seventh month (28 to 30 weeks), the eighth month (32 to 34 weeks), and approximately a week or so just prior to the expected date of delivery (37 to 39 weeks). Pelvimetry and cephalometry studies were also made just before delivery.

From the accompanying table it will be seen that at approximately five months of pregnancy, 74 cases were cephalic presentations, and 26 were not in the normal polarity (normal polarity being a parallelism of the fetal axis with the long axis of the patient, the cephalic pole presenting at the inlet). Repeated observations of the 74 cephalic presentations at the intervals indicated above revealed no change in presentation throughout the entire course of gestation. Although DeLee cited a case which changed from a cephalic presentation lodged deeply in the pelvic excavation to a breech presentation late in pregnancy, such an occurrence is probably a rarity; and reports of such rotations should be supported by x-ray evidence. On the other hand, it is commonly accepted that changes in fetal position are variable and frequent, and the x-rays of this series support this view without question.

Closer scrutiny of the 26 cases with errors in polarity reveals interesting changes. Two of these had been found to be in the transverse presentation at five months of pregnancy. By the end of the seventh month these two fetuses had rotated to become vertex presentations and remained so until delivery. In addition, 16 of the remaining 24 breech presentations had rotated to cephalic presentations in the same period of time. At the end of the eighth month of gestation, one more breech had rotated to vertex but seven remained in the breech presentation deeply placed in the pelvic cavity.

TABLE I. SERIAL X-RAYS OF THE ABDOMEN DURING THE COURSE OF PREGNANCY STUDIED FOR CHANGES IN FETAL POLARITY

	5TH MONTH (18 TO 22 WEEKS)	7TH MONTH (28 TO 30 WEEKS)	8TH MONTH (32 TO 34 WEEKS)	ONE WEEK BEFORE TERM (37 TO 39 WEEKS)
Cephalic presentation	74	92	93	99
Breech presentation	24	8	7*	1
Transverse presentation	2	0	0	0

*After the completion of eight full months of gestation, seven pregnancies remained in the breech position deep in the pelvic excavation. Six of the seven breech presentations were rotated manually to vertex by external version at this time, and one breech allowed to continue to term since an elective low-flap cesarean section was to be done in this instance for another indication.

At this time external versions were performed on six of the remaining seven breech cases, and x-rays taken subsequent to the versions showed cephalic presentations.* These six cases continued along as vertex presentations and were delivered as such. The remaining case in which no version was attempted was allowed to remain in the breech state until one week before term when a planned elective cesarean section (low flap) was performed for cervical fibroid blocking the passageway. The fetus was delivered easily by podalic extraction at operation.

*It is not within the province of this short paper to discuss the advantages and disadvantages of external version. However, one fact must be stated at this time which is entirely relevant. Unless the exact position of a breech, or transverse presentation is outlined by x-rays, and the proper application of the laws of physics applied in making pressure on the fetus in utero, the results of external version will be sadly disappointing. A thorough study of external version will be presented in a subsequent paper.

Summary

Radiographic antepartum polarity studies were made at periods throughout the course of pregnancy in 100 unselected primiparous women. At five months of gestation, 74 cephalic presentations were found and 26 errors in polarity were disclosed (24 breech and two transverse). After 8 months of pregnancy, 19 of the 26 faulty presentations had rotated spontaneously to cephalic presentation. At this time 6 of the remaining 7 breech cases were rotated by external version, while the remaining breech presentation was allowed to go to term as a breech in view of the planned elective cesarean section (low flap) for cervical fibroid blocking the passageway. At term 99 per cent of the cases were normally delivered as vertex presentations, and the one child delivered by podalic extraction in the course of the elective cesarean operation.

Conclusions

Repeated radiologic studies during the course of pregnancy are a valuable method of learning the exact intrauterine changes in polarity of the fetus.

Up to one month prior to delivery, 73 per cent of errors of polarity (breech and transverse presentations) will rotate spontaneously to the cephalic presentation.

If by eight full months of gestation spontaneous version has not occurred, it is suggested that external version be attempted to effect a normal polarity, since at this stage with the breech deep in the pelvis spontaneous version is unlikely.

Of 100 primiparous women who presented radiologic evidence of 26 errors in polarity early in pregnancy, 99 per cent were finally delivered normally with the vertex presenting. One breech which did not rotate by the eighth month was allowed to continue to term as such, since an elective cesarean section was to be performed for another indication.

HYPERTHYROIDISM AND PREGNANCY

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MOST authors agree that hyperthyroidism is a comparatively infrequent complication of pregnancy. Portis and Roth[1] showed an incidence of 1.4 per cent, while Javert[2] reported 0.076 per cent. In the Bronx Hospital, over a period of six years, 15,864 pregnant women were admitted. Of these, only 12 or (0.075 per cent) showed abnormal hyperactivity of the thyroid gland. These cases were divided clinically, into diffuse exophthalmic goiter (3 cases), toxic adenoma (1 case), and hyperthyroidism (8 cases). The symptoms of hyperthyroidism developed during pregnancy in 7 cases, antedated the pregnancy in 3 cases, while 2 cases dated their symptoms to a previous pregnancy.

Of the 12 patients with hyperthyroidism, 8 went to term, 1 had operative interference in her thirtieth week of gestation, and 3 aborted. Of the 3 abortions, two cases were performed for therapeutic reasons, on a cardiac basis. One of the therapeutic abortions was performed on a patient with a history of cardiac collapse during her last delivery. The other therapeutic abortion was started by x-ray, on a class iii cardiac near menopause; but had to be completed by operative measures a month later because of bleeding. One patient aborted spontaneously in her fifth month of gestation, six weeks following a subtotal bilateral thyroidectomy.

There were 9 multiparas and 3 primiparas; and the average age was 30.9 years.

Toxemia of pregnancy was observed in 5 cases (or 55.5 per cent) of the cases reaching viability or term.

The average basal metabolic rate of plus 40 per cent was reduced by hospitalization to an average of plus 23 per cent.

The type of delivery revealed seven (or 77.7 per cent) spontaneous deliveries. Two were operative deliveries, one a midforceps, and the other a Voorhees' bag, followed by version and breech extraction for central placenta previa.

Subtotal bilateral thyroidectomy was done in four cases, three during pregnancy, and one 4½ months following delivery. The first patient, operated on at the end of her second month of her pregnancy, had a spontaneous abortion 2½ months later. The second patient was thyroidectomized in her third month of gestation, went to term, and delivered spontaneously of a Mongolian idiot. Interestingly enough, in her previous pregnancy, she also delivered a Mongolian idiot. The third patient had a therapeutic abortion done at the end of the second month of a previous gestation. She promptly became pregnant two months later, and her symptoms became aggravated. This time she had a subtotal thyroidectomy near the end of her third month of gestation,

and then delivered spontaneously at term. The fourth case is now presented in more detail.

Case Report

Patient B. D., aged 39, was a gravida ii para i. Her last menstrual period was July 28, 1940, and her expected date of confinement was May 5, 1941. She was admitted to the Bronx Hospital on February 16, 1941, because of painless bleeding, 2½ months before term.

Past History.—Five years previously, she had a normal spontaneous delivery of an eight months' premature baby, that is living and well. Three years ago, she came to her family doctor because of a relative sterility, and on examination, was found to have hyperthyroidism with a basal metabolic rate of plus 60 per cent. Operation was suggested, but the patient refused.

She was given iodides, with a reduction of her basal metabolic rate to plus 48 per cent. Iodides were continued and seemingly controlled the severe symptoms of her hyperthyroidism. In July of last year, she became pregnant. At that time, her blood pressure was 135 systolic over 80 diastolic, with a blowing systolic at the right base of the heart. The pelvic measurements were ample. During her prenatal course, the blood pressure varied from 135 systolic over 80 diastolic to 150 systolic over 100 diastolic, with the urine consistently negative.

Present History.—Patient began to stain two weeks before admission to the hospital, for which she was kept in bed. On February 15 the day before admission, she had active bleeding for a short while. The following day, she bled profusely and was told to come to the hospital immediately.

On admission, the red blood count was 3½ million with 78 per cent hemoglobin. Slight bleeding was present. The patient was typed and the donor ordered to be ready. The height of the fundus was three fingers above the umbilicus. No fetal heart was heard.

Vaginal examination revealed a vertex presentation, the cervix 1½ fingers dilated, and the presence of a central placental previa.

Because it was scarcely likely that the fetus was viable, cesarean section was considered not indicated, first, because of the period of gestation, and secondly, the character of the bleeding. Under light anesthesia, a No. 4 bag was readily introduced into the cervix in front of the placenta, without any additional bleeding, and the vagina was packed with iodoform gauze. Sedation and a transfusion of 500 c.c. of citrated blood was given. The patient was watched all night for bleeding and other physical signs, with the pulse and blood pressure taken at frequent intervals.

The next morning the bag was in the vagina and the cervix was four fingers dilated, and readily dilatable. The edge of the placenta was approached to the patient's left, and separated. The membranes were then ruptured. The posterior foot was grasped, and an internal podalic version and extraction was performed, with delivery of a stillborn female, weighing 3½ pounds. The placenta followed the head as it was delivered. The uterus and the vagina were packed with fifteen yards of iodoform gauze, which was removed in forty-eight hours.

One-half hour following the patient's removal to her room, her pulse suddenly rose to 180. There were extreme restlessness, marked flushing, and an anxious facies. Her blood pressure was 140 systolic over 0 diastolic. No diarrhea, no jaundice, and no mental symptoms were present. Medical consultation suggested we were dealing with a thyroid

storm, and advised, (1) sedation, (2) 1,000 c.c. of 10 per cent glucose intravenously with sodium iodide or Lugol's solution added, (3) oxygen inhalation, and (4) cold packs or ice bags to head and body. These instructions were followed.

The following day, the temperature ran up to 103° F., but gradually came down to normal in the next four days, with the pulse gradually slowing to 100.

She was discharged on the tenth day post partum with the hyperthyroidism apparently under control, the temperature normal, the pulse rate 90, and the general condition good. Since leaving the hospital, her basal metabolic rate rose to plus 60 per cent. Four and one-half months later, she re-entered the hospital and had a subtotal bilateral thyroidectomy performed. At her last visit, one year later, patient was in excellent condition.

Discussion

Bothe[3] showed the experimental evidence of the relation of the anterior pituitary hormone to the activity of the thyroid gland, whose function is the production of a secretion which activates heat and energy production by regulating the rate of oxidation in the cells throughout the body. Mussey[4] states that the thyrotropic hormone of the anterior lobe of the pituitary stimulates the thyroid gland to hyperplasia and the production of thyroxin, and causes the release of stored colloid. Overproduction of thyroxin tends to develop an antihormone in the body, which depresses the thyrotropic output of the anterior lobe of the pituitary. The thyrotropic content of the pituitary, therefore, becomes inversely proportional to the thyroxin output of the thyroid gland. Sufficient iodine is also necessary to enable the thyroid gland to discharge all the thyroxin it produces. If the amount of ingested iodine is insufficient for the physiologic demand of the increased metabolism during pregnancy, the appearance of colloid or simple goiter may result. This result may be hypothyroidism in the mother, and if the degree of hypothyroidism is sufficient, it may cause miscarriage or the development of colloid goiter or cretinism in the infant.

On the other hand, if there is a sustained stimulation of the thyroid in conjunction with certain unknown factors, a condition of hyperthyroidism develops. This may occur during pregnancy, or more commonly the woman may become pregnant while the hyperthyroidism exists. Occasionally, cases of what was thought to be toxemia of pregnancy have turned out to be the result of an overactive thyroid gland. Javert, however, states that the high incidence of toxemia of pregnancy (76 per cent) in his series of hyperthyroidism in pregnancy seems significant, and raises the question of a common factor in toxemia and in thyrotoxicosis.

The diagnostic features of hyperthyroidism in pregnancy are practically identical with those of hyperthyroidism in the nonpregnant state. But the subsequent course frequently assumes a different clinical picture. The majority of patients show either a stationary condition, or an amelioration of symptoms, and only a small number show a progression as the gestation continues.

With regards to treatment, all authors agree that it is the thyrotoxicosis and not the pregnancy which should be interrupted. Therapeutic abortion is not indicated, except in rare instances, as in Portis and Roth's case, where multiple operations on the thyroid precluded the likelihood of a further successful operation. Mild hyperthyroidism complicating pregnancy may be controlled by medical management. The use of iodine early in pregnancy has reduced the incidence of hyperthyroidism. If the medical treatment does not produce the proper result, Bothe, Mussey, and Portis and Roth advocate surgical interference on the thyroid, regardless of the period of gestation. Javert, however, feels that with proper treatment patients with hyperthyroidism may safely go through a pregnancy and sometimes even be benefited thereby. Hospitalization for evaluation and stabilization may be necessary several times during the antepartum course. As a general rule, he feels the best time for operation on the thyroid, is in the first postpartum year, so that the effects of pregnancy on the thyroid gland are no longer present. He does admit, however, that thyroidectomy may be performed in individual cases.

Conclusions drawn from these comments seem to indicate that each case should be individualized. If possible, the pregnant woman with hyperthyroidism should be carried to term, and only exceptional cases, that grow progressively worse, in spite of adequate and intensive medical treatment, should be thyroidectomized. It should be a dictum that the pregnancy itself should not be interfered with, unless there is an obstetric reason.

Summary

1. There were 12 cases of hyperthyroidism in 15,864 pregnant women, an incidence of 0.075 per cent.

2. Therapeutic abortions were done in 2 cases, an incidence of 16.6 per cent.

3. There were 9 multiparas and 3 primiparas, with an average of 30.9 years.

4. Toxemia of pregnancy was observed in 5 cases, or 55.5 per cent of the cases reaching viability or term.

5. The average basal metabolic rate of plus 40 per cent was reduced by hospitalization to an average of plus 23 per cent.

6. Subtotal bilateral thyroidectomy was done in 4 cases, an incidence of 33.3 per cent.

7. A severe case of hyperthyroidism during pregnancy, complicated by a central placenta previa, is presented.

8. Pregnancy and hyperthyroidism are discussed.

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HEMORRHAGE AS THE MOST IMPORTANT CAUSE OF MATERNAL DEATH IN BROOKLYN, CITY OF NEW YORK

An Analysis of the Puerperal Deaths of 1943*

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IN THE course of our inquiry into the circumstances of every maternal death in Brooklyn, we have reviewed at monthly meetings, to which all physicians are invited, those cases which appear to teach valuable lessons to general practitioner and obstetrician alike. In 1937, and for a short time thereafter, we discussed every death, and clearly our intention was to assign preventability and fix responsibility. This practice was abandoned partly because we could not agree upon the criteria of preventability, but largely because we became aware of the enormous educational value of the common obstetric conference. Those who attend these meetings will testify to their teaching value. It is true that interest has never been what it might be, since the general practitioner group has always been poorly represented, unconvinced that group discussion of actual cases of maternal death is a worth-while method of learning. Yet, what could be better or easier? Widespread knowledge of the principles of obstetric practice is vital, if the problems which confront us every day are to be solved rightly. True, the art of obstetrics cannot be taught by round table discussion any more than it can be learned from a textbook, yet discussion of the details and implications of maternal deaths can readily be converted into reduced mortality.

Once every year, a complete case study is presented to the medical profession at an open meeting of this Society. I believe that we have developed a simple method of postgraduate education which, if fully effective, should prove to be highly developed preventive medicine. Our puerperal mortality experience is good, and I like to feel that we have helped to reduce the death rate, yet perhaps we are but participating in the extraordinary decline in puerperal death rates going on in no less than forty-one states.

In the United States during 1942,[1] the latest year for which figures are available, the number of live births increased 11.8 per cent, yet the number of puerperal deaths decreased from 7,956 in 1941 to 7,267. The national maternal death rate was 2.6 per 1,000 live births, the lowest rate yet recorded.

Through the personal interest of Mr. Thomas J. Duffield, Director of the Bureau of Records and Statistics of the Department of Health, City of New York, figures for Brooklyn for 1943 have been tabulated at this early date, and transcripts of death certificates sent us throughout the year have been checked by the Visiting Nurse Association of Brooklyn.

The number of live births occurring in Brooklyn during 1943 was 49,423, and the total number of births was 52,352. The puerperal rate based on 55,660 reported terminated pregnancies and standardized for color, on the basis that each borough had the same proportion of colored

*Read at a meeting of the Brooklyn Gynecological Society, May 5, 1944.

pregnancies as the city as a whole is 20.3. This rate for the entire City of New York is 20.1. In 1942, the Brooklyn rate was 20.7. If this rate were computed on the basis of live births, as is the national figure, the rate would be 22.7. The rate, however, is not a true measure of the risk of pregnancy, for deaths from abortion are included, while pregnancies terminating in abortion are not.

In 1943, 121 women died of causes associated with pregnancy and childbirth; 9 of these deaths were assigned to nonpuerperal causes, and 112 cases were assigned primarily to puerperal causes. In the puerperal group of 112 cases, 101 women were white and 11 colored.

Nonpuerperal Causes of Death (9)

It is not generally appreciated that preventive programs cannot be planned without consideration of the nonpuerperal causes of death, primary as well as secondary. Nephritis was assigned as the cause of death in 4 cases, yet in one of these, death was really due to eclampsia and cesarean section. In 2 cases, death was due to severe cardiac disease; both women died undelivered without any prenatal care whatever; one was found moribund at home, and the other died shortly after admission to the hospital.

Cardiac Disease.—Among the secondary nonpuerperal causes of death, cardiac disease was reported in 17 cases, but in not all of these was it actually present. In certifying obstetrical death, mention of circulatory failure, vasomotor collapse, cardiac decompensation, heart failure, acute cardiac dilatation and acute or chronic myocarditis unduly weights statistics with faulty figures, for the vital statistician will assign death to heart disease. In one case, for example, ascribed to acute myocarditis, death was due to severe postpartum hemorrhage which followed unattended delivery of a woman who had been long in labor. In another case where the patient was found in shock, with bed linen soaked with blood, two hours after delivery, death was said to be due to "postpartum hemorrhage and cardiac decompensation."

Death was due to subacute bacterial endocarditis in 4 cases. In one case death followed home delivery in the fifth month. In another case the death certificate was well written: "Subacute bacterial endocarditis, streptococcus viridans, secondary to rheumatic heart disease. Contributory: pregnancy 5½ months; embolism from heart to brain; left hemiplegia." These deaths were assigned to puerperal causes.

In 3 cases associated with operative delivery, heart disease contributed to death. The sequence of events is stated:

CASE 1.—Mitral stenosis, decompensated one week before admission to the hospital with membranes ruptured 48 hours; dyspnea grew worse and pulse rate rose to 140 She was not in labor. Under spinal anesthesia, the cervix was dilated manually, and she was delivered with forceps; postpartum hemorrhage; death during transfusion.

CASE 2.—Primigravida with severe heart disease, excellent prenatal care, had not decompensated during pregnancy. Elective cesarean section at term under caudal anesthesia; death from heart disease one day later.

CASE 3.—Para ii, who had refused to enter the hospital several times during pregnancy, was delivered spontaneously in the hospital after quick labor. Death in heart failure 5 days later.

Pre-eclampsia and eclampsia complicated serious cardiac disease in 2 patients delivered by cesarean section; death from heart disease weeks later.

In addition to the 2 deaths assigned primarily to heart disease, 3 more young women, who had no prenatal care, died of cardiac disease during the last trimester. One died at home after delivering herself unattended; and 2 others who were admitted to the hospital in heart failure, died of hemorrhage.

Heart disease played an important part in the deaths of 13 women, or 10 per cent of the total number of 121 deaths associated with pregnancy and childbirth.

Pelvic Tumors.—Fibroids and ovarian tumors were associated with death in 5 cases. Brief data indicate controllable factors:

CASE 1.—Multiple myomectomy during laparotomy for ruptured ectopic gestation was followed by peritonitis.

CASE 2.—Cesarean hysterectomy for fibroids and an endometrial cyst were followed by wound disruption and peritonitis.

CASE 3.—Myomectomy in the course of classical cesarean section was followed by intestinal obstruction.

CASE 4.—Cesarean section with removal of an ovarian teratoma discovered 5 hours after onset of labor was followed by pulmonary embolism 12 days post partum.

CASE 5.—An ovarian cyst found after 14 hours of labor was readily removed at laparotomy, and delivery then easily effected with forceps. Death was due to secondary hemorrhage from the tumor pedicle.

Puerperal Deaths (112)

The official tabulation of all the deaths assigned to puerperal causes follows: (See Table I.)

TABLE I. CAUSES OF HEMORRHAGE

NUMBER	CAUSES	PRIMARY	SECONDARY
140	Abortion with infection	10	
141	Abortion without infection	9	2
142	Ectopic gestation	9	
143	Hemorrhage of pregnancy	1	
144	Toxemias of pregnancy	4	2
145	Other diseases and accidents of pregnancy	4	3
146	Hemorrhage of childbirth	20	2
147	Infection	21	1
148	Puerperal toxemias	14	4
149	Other diseases and accidents of childbirth	11	22
150	Other unspecified	9	
	Total	112	36

Comparison of the major causes of death with those of the preceding year is made below: (See Table II.)

TABLE II. COMPARISON OF MAJOR CAUSES OF DEATH 1942 AND 1943

RUBRIC	CAUSES	1942	1943
140 and 141	Abortion	21	19
142	Ectopic	6	9
143 and 146	Hemorrhage	15	21
144 and 148	Toxemia	24	18
147	Infection	27	21
145 and 149	Accidents	14	15
150	Other	7	9
	Number of puerperal deaths	114	112
	Reported terminated pregnancies	56,247	55,660
	Rate	20.7	20.3

Deaths in Early Pregnancy

Abortion.—Abortion was responsible for 19 deaths, or 17 per cent of all the deaths from puerperal causes. This is approximately the same as the national rate. In the infection group, nearly all were induced. Deaths from toxemia, hemorrhage and trauma which occur before the twenty-eighth week of gestation (7 lunar months) are not assigned to their specific causes, but to abortion. Two cases will illustrate:

CASE 1.—History of hypertension for three years; aged 24; no prenatal care. Admitted to hospital with blood pressure 220/160 and blurring of vision. Abdominal hysterotomy under general anesthesia was followed by hemorrhage and shock; death from septicemia 3 weeks later.

CASE 2.—Multipara, in the sixth month of pregnancy, was admitted to the hospital in profound shock following profuse hemorrhage due to ablatio placentae. Morphine and plasma were administered promptly, and the membranes were artificially ruptured. Delivery expedited by pituitrin was rapid, and she received 750 c.c. of blood following expulsion of the placenta. Her condition improved markedly, but she died of pulmonary edema a week later.

In the absence of cardiac disease, hemorrhage caused death in early abortion. One case is interesting.

CASE 1.—Bleeding profusely, a patient was admitted to the hospital in profound shock. After a 3 months' placenta had been removed from the cervix, bleeding ceased. She received plasma and two blood transfusions, but died 9 hours later, blood pressure never rising above 60/40.

There were 5 deaths in the abortion group directly due to hemorrhage and shock, and 3 more in which profuse hemorrhage was reported.

Ectopic Gestation.—There were 9 deaths from ectopic gestation, while there were 6 in 1942, and only 3 in 1941. The optimum time for operation passed in 6 cases due to long delay in diagnosis. Two patients admitted to the hospital in severe shock were not operated upon, one living for three hours without any improvement after large transfusion. In another case peritonitis followed incidental multiple myomectomy. And in one case death occurred as a result of spinal anesthesia while the peritoneum was being opened.

Toxemia

As hitherto, in no case did toxemia or eclampsia fail of mention on the certificate of death. All our experience has been to the contrary in the case of infection, and in hemorrhage particularly. The number of deaths was less than in 1942, but more than twice as great as in 1941.

In the total number of 24 cases in which toxemia was mentioned, 5 cases were found in which this diagnosis does not appear to be warranted. In 9 cases of eclampsia, 3 women died undelivered, and 2 were subjected to cesarean section after the onset of convulsions. With notable exceptions, inadequate or no prenatal care as well as formidable operative procedures were common, yet as might be expected, excellent prenatal care and spontaneous delivery did not prevent death. Shock occurred in some cases without trauma or undue loss of blood.

To illustrate the importance of good prenatal care and the influence of hard delivery upon the outcome, the salient facts in certain cases of pre-eclampsia are briefly cited.

CASE 1.—Admitted to hospital with blood pressure 226/110 and history of severe bleeding in the seventh month. At term, her complaints of blurred vision, headache and vomiting were ignored until she became stuporous, and neighbors called an ambulance.

CASE 2.—Classical cesarean section after 90 hours of labor with membranes ruptured; death from peritonitis.

CASE 3.—Primigravida 3 days in labor; failure of midforceps and forceps rotation; craniotomy; shock.

CASE 4.—Primigravida induced by rupture of membranes; after 12 hours of labor, cervical incisions under general anesthesia taken very badly, hemorrhage and shock; uterus packed. Cardiac stimulants, adrenalin, and several doses of ergotrate without control of bleeding; no transfusion.

Infection

In the group of 21 cases assigned to infection, it is of particular interest that 11 cases of pulmonary embolism are included. Cesarean section contributed to death in 8 cases. In 3 cases said to be due to pulmonary embolism, death was due to general anesthesia (1 case), massive retroperitoneal hemorrhage following lower segment cesarean section (1 case), and rupture of the uterus (1 case). In all but 2 cases, death occurred late, from the twelfth day to fourteen weeks post partum.

Cesarean Section

Cesarean section contributed to death in 30 cases, 27 per cent of the total number of puerperal deaths, or 36 per cent of the deaths, if abortion and ectopic gestation are excluded. In 9 cases, death was assigned to this cause, and to other causes in 16 cases as follows: hemorrhage (6), infection (7), toxemia (2), and nephritis (1). There were 5 additional cases in which this operation was reported and not tabulated, other causes receiving preference. In 2 cases of cesarean hysterectomy death was due to wound disruption and peritonitis. One case in which cesarean section had been planned, but the uterus found to be ruptured is not included.

In 11 cases, there had been no labor. In 6 elective operations performed because of previous cesarean section, death was due to peritonitis (1 case), massive pulmonary collapse (1 case), and hemorrhage (4 cases). An example follows:

CASE. After elective lower segment operation under general anesthesia, the patient was returned to her bed in shock. Bleeding continued for five hours. Transfusion, attempted several times, was successful for only 300 c.c. of blood.

The lower segment operation was performed after labor of 48 hours (2 cases) and 72 hours (1 case) and in one case classical cesarean section was performed after 90 hours of labor. In several cases, intraperitoneal and intravenous chemotherapy was administered.

In the entire group of 30 cases hemorrhage was severe or caused death in 11 cases, though general anesthesia was a contributory cause in 3 of them. Death was due to infection in 9 cases. In 2 cases death attributed to infection was reassigned to hemorrhage. For example:

CASE 1.—Cesarean section for placenta previa after profuse bleeding at home. Shock occurred during removal to bed. Plasma and intravenous glucose were administered. Death from peritonitis fifteen days later.

Hemorrhage

By this time it has become clear that a "broad stream of blood" runs through these statistics. Officially 21 cases were assigned to hemorrhage. Repeated antepartum hemorrhage at home, placenta previa and ablatio, long labor, unrecognized transverse presentation, postpartum hemorrhage, retained placenta and ruptured uterus are included. Incision or manual dilatation of the cervix, version and extraction, forceps, craniotomy and even episiotomy and spontaneous delivery are reported in this group.

In some cases proper shock therapy was prompt though ineffective, probably because shock had existed too long before admission to the hospital. In a great many cases, plasma, glucose solutions, cardiac stimulants or comparatively little blood, often very late, were relied upon for replacement of lost blood. In many cases the uterus was packed, yet bleeding did not stop. And sometimes consultants gave strange advice.

Space will not permit even a brief report of all the cases in this group, though every case is highly instructive. A few will suffice.

CASE 1.—Unattended delivery after 24 hours of labor was followed by profuse hemorrhage. After the placental stage, the uterus repeatedly relaxed. Intravenous glucose therapy was attempted, but veins could not be entered. Death from shock in one hour.

CASE 2.—Para xv, no prenatal care, delivered herself at home. One hour later she was found in profound shock.

CASE 3.—Following profuse hemorrhage at home from placenta previa, patient entered the hospital exsanguinated with a pulse of 160. She was given morphine, 500 c.c. of plasma, 2,000 c.c. of glucose solution and cesarean section was rapidly performed under ether anesthesia. Her condition was poor throughout, so she was transfused with 500 c.c. of blood immediately afterward, hemorrhage continuing. Profuse hemorrhage followed removal to bed.

CASE 4.—Ten days post partum, after sudden hemorrhage estimated at 1,000 c.c., blood pressure fell to 84/46, and 500 c.c. of blood were administered. Examination showed a dilated cervix and retained tissue. During its removal, two days later, profuse hemorrhage recurred. Vaginal packing and 500 c.c. of blood followed. Upon removal of the packing the next day, profuse hemorrhage estimated at 800 c.c. occurred. Then 1,000 c.c. of plasma and 750 c.c. of blood did not save her.

CASE 5.—Spontaneous delivery followed by profuse post-partum hemorrhage. Saline and plasma were administered. One hour later, it was thought that her condition would not permit removal of the placenta. Death one hour later with placenta retained.

In case reports hemorrhage was so commonly encountered, that it would appear to be wise and necessary to revise official figures in order to learn its true importance. Shock is not included in this revision unless hemorrhage was mentioned. Nor are cases with blood loss said to be 500 c.c. included; nor any case unless hemorrhage was reported as severe or profuse. Nor is a patient with severe leucemia who died from severe postpartum hemorrhage from the genital tract as well as from her nose and throat, or 2 women with severe anemia who had no undue bleeding, yet died of shock shortly after delivery. Deductions for hemorrhage are made in the following table. (See Table III.)

Obstetrical death is commonly the result of several causes, rarely one, and actually it is very often impossible to assign death to one cause.

TABLE III. HEMORRHAGE AS A CONTROLLABLE FACTOR

RUBRIC	CAUSES	CAUSES AS OF CERTIFICATE OF DEATH	HEMORRHAGE FACTOR AS OF CASE REPORTS
140, 141	Abortion	19	8
142	Ectopic	9	9
143, 146	Hemorrhage	21	21
144, 148	Toxemia	18	4
147	Infection	21	8
145, 149	Accidents	15	8
150	Other	9	2
	Total	112	60

The accuracy and value of statistical deductions depend upon the quality of the information furnished by the certificates of death. Dunn[2] says, "The cause of death information given on the death certificate is, for the most part, fairly reliable. . . . Although a number of notable studies have been made on the accuracy of medical diagnoses, there is an unfortunate lack of national statistics on the subject. All of these investigations are extremely limited in scope, since they are based upon comparisons of autopsy and clinical records in certain hospitals."

Numerous controllable factors are indicated in this study. The scope of this paper will not permit discussion of the importance of proper application of the basic concepts of good obstetric practice. Certainly casual obstetricians should not make weighty decisions thoughtlessly or hastily, nor should they attempt operative procedures beyond their skill without consultation or assistance. That those upon whom they lean for advice and support should be well qualified, is obvious.

Though many women in Brooklyn seek no prenatal care at all, it is still true that not every physician realizes the importance of pre-eclampsia, and the necessity of hospitalization for its observation and treatment. Nor are we all convinced of the gravity of the association of heart disease and pregnancy, and of the need for continuous hospital care, no matter how long, after cardiac decompensation.

Every obstetric patient should have her blood typed, with determination of her Rh factor, early in pregnancy, perhaps at the time blood for her Wassermann test is taken.

If only for its own good, every hospital should insist upon observance of good rules for consultation in obstetric emergencies. And the hospital should see to it that facilities for blood transfusion are satisfactory. It is true that plasma has been made more generally available, yet more and more, it becomes apparent that plasma will not save life if blood loss has been great. Undue confidence is had in plasma. Our Brooklyn hospitals need blood badly. It is our hope that the American Red Cross will lend us a helping hand.

In Brooklyn, hemorrhage is the outstanding controllable factor in maternal mortality. We became acutely aware of this in 1940,[3] and it has been so ever since.[4, 5] In 1943, it was a significant factor in 53.6 per cent of all our puerperal deaths. Its importance cannot be overestimated. Our experience, as of our own figures, as shown in the following table. (See Table IV.)

Reviewing the maternal mortality statistics of the United States for 1941, Yerushalmy[6] points out that "Infection was the leading cause of death (3,034—38 per cent) while the other two major groups of causes were each responsible for one quarter of the maternal deaths. Hemor-

TABLE IV. MAJOR CAUSES OF MATERNAL DEATH
BROOKLYN 1937 TO 1943

YEAR	INFECTION	TOXEMIA	HEMORRHAGE
1937	27	26	29
1938	27	18	27
1939	30	12	14
1940	18	10	28
1941	10	8	20
1942	25	22	30
1943	13	14	60
Total	150	110	208

rhage, trauma or shock was the cause of 2,032 of the maternal deaths, and toxemias were responsible for 2,031.

If the national figures for these three great causes of death in 1942 are compiled in exactly the same way, we find that the number of deaths from infection was 2,618, from toxemia 1,807, and from hemorrhages 2,018. The percentage reduction in infection was 10 per cent, in the toxemias 11 per cent, and in the hemorrhage group only 0.005 per cent. This resistance of hemorrhage is of great significance.

For these national figures it must be understood that only certificates of death were available, and in a great many of these, the basic data were so meager that little more than the fact of pregnancy could be established.

It has been said over and over again, that infection as the most common cause of death is the most important. Definitely the outstanding controllable factor in Brooklyn, hemorrhage is no doubt far more common everywhere than indicated by its statistical frequency. Preventive measures for reduction of maternal mortality will produce greater results, if emphasis is placed on hemorrhage, rather than infection. At present, hemorrhage is the most important cause of maternal death, and probably the most common as well.

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32 REMSEN STREET

Department of Reviews and Abstracts

WEIGHT CHANGES AND WATER BALANCE IN NORMAL AND TOXIC PREGNANCY

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WEIGHT changes in pregnancy have been extensively studied because many investigators have felt that excessive gains in weight are correlated with certain complications of pregnancy, parturition and puerperium, especially with late toxemia (pre-eclampsia and eclampsia). In reviewing the literature, one finds that what is essentially a statistical problem has very seldom been subjected to statistical operations other than to determine the average weight change in relation to the incidence of the complication (s) under analysis. Furthermore, the data given are usually so few as to preclude any analysis by the reader. Curiously, the *average* gain is frequently calculated and then implicitly taken as the *upper normal,* thereby negating the normality of half the normal series from which the average was determined.

Weight Changes in Normal Pregnancy

There have been four approaches to the problem as to what constitutes normal weight change in pregnancy. 1. The average change during normal pregnancy has been determined; this has been the most popular method. 2. The weight lost at delivery and in the puerperium has been determined. The assumption is that a woman having a normal weight gain in pregnancy will return nearly to her prepregnancy weight (as will many patients with abnormal degrees of edema). 3. The "reproductive weight" has been estimated by adding together the weights of the conception product, and the increase in weight of the hypertrophied uterus and adnexa, and of the breasts. To this, later authors have added factors for the increased blood volume, and made varying estimates for physiologic edema, nitrogen storage, and other "necessary" changes. 4. A few studies of weight gain have been made in other pregnant animals.

In general, the first method gives the highest average. The second and third methods have checked somewhat better at about 5 pounds less than by the first. Different estimates and guesses as to the magnitude of changes in the maternal organism, not all of which are appreciated, introduce a considerable variation in the third approach. The few studies in other animals show a net gain to the maternal tissues, but it is uncertain whether a strictly proportionate change can be assumed for the human organism. The third and fourth methods will not be discussed except incidentally in the section on what constitutes the weight gain in pregnancy.

Weight Changes During Pregnancy.—Many of the available data bearing on the weight gain in pregnancy are not strictly comparable. Some series have included toxemias while others have rigidly excluded them; some have excluded patients showing edema and others have not.

TABLE I. SUMMARY OF WEIGHT GAINS IN NORMAL PREGNANCY

AUTHOR	YEAR	LOCALITY	CASES	WEIGHT GAIN, IN POUNDS				RATE OF GAIN IN LAST TRIMESTER POUND/WEEK	WEIGHT GAIN RELATED TO		
				FIRST TRIMESTER	SECOND TRIMESTER	THIRD TRIMESTER	TOTAL		WEIGHT	AGE	PARITY
Gassner[22]	1862	Munich	8 to 89					1.03	Heavy gain more		Multiparas more
Góth[23]	1881	Kolozsvar	80					0.32	Heavy gain more		Multiparas gain more
Baumm[2]	1887	Munich	16					0.98	Heavy—more		
Krüger[40]	1909	Halle	10 to 57			13.6		1.02	Heavy—more	Old more	Multiparas more
Zangemeister[66]	1916	Marburg	300			12.5		0.88	Heavy—more		No
Lorenzen[44]	1922	Jena	78					1.06	Heavy—more	Young more	Multiparas more
Davis[15]	1923	Milwaukee	150				21.0				
Kemper[34]	1924	Marburg	22 to 345		6.8	9.4		0.71	Heavy—more	Young more	Multiparas more
Hannah[28]	1925	Dallas	236				13.3				Primiparas more
Randall[56]	1925	Rochester	300	3.5	7.9	11.1	22.5	0.85			Primiparas more
Kerwin[37]	1926	St. Louis	127 to 260		10.1	6.4		0.47			
Slemons and Fagan[60]	1927	Los Angeles	500				16.5				
Trillat[62]	1928	Lyon	252			11.0	21.1	0.82	No		Multiparas more
Plass and Yoakam[52]	1929	Iowa City	48				37.4				
Rowe, Gallivan and Matthews[57]	1931	Boston	77			13.4		1.01			

*Gains for the last 6 months of pregnancy.
P = Primiparas.
M = Multiparas.

Bingham[7]	1932	East Orange	1,288	2.9	10.0	7.0	19.9	0.53			
Siddall and Mack[58]	1933	Detroit	624			12.8		0.96	No	Young more	No
Hanley[27]	1934	Los Angeles	482				22.0*				Primiparas more
Lawson[42]	1934	Washington	220	0.0	14.0	10.5	24.5	0.79			
Cummings[13]	1934	Ann Arbor	937	0.5	13.1	10.5	24.1	0.79			No
Harding and Van Wyck[29]	1934	Toronto	719					1.25(?)			
Wodon[65]	1935	Brussels	311				20.0%		Heavy gain more		
Frýza[21]	1937	Ostravě	344					0.95			
Evans[20]	1937	Cornwall	159			8.4		0.63			No
McIlroy and Rodway[46]	1937	London	1,000			9.9		0.74	Light—more	Young more	No
Pugliatti[55]	1937	Milan	200				22.0		Heavy—more	Young more	Multiparas more
Bray[8]	1938	Duluth	69				23.7		No	No	No
Cova[12]	1938	Turin	?					0.77[P]			Multiparas more
								1.08[M]		Young more	
Mauks[48]	1939	Budapest	208			9.2	22.0	0.70			No
Bertini[5]	1939	Turin	228				24.6*	1.10[P]			Multiparas more
								0.73[M]			
Stander and Pastore[61]	1940	New York	2,502	2.7	(11.4%)	(10.5%)	(24.1%)	(0.75%)	Heavy—more		No
					14.6	13.4	30.7	0.96			
Granger[24]	1941	Rockville Center	100				23.3				
Beardsley[3]	1941	Eugene	200	0.8	12.4	11.6	24.8	0.87	Light—more		Primiparas more
Kuo[41]	1941	Peiping	200	1.0	12.3	10.0	23.3	0.75	Light—more	Young more	Primiparas more
Dieckmann[16]	1941	Chicago	?				24.0	0.99			
Waters[63]	1942	Jersey City	3,230	3.2	8.0	12.0	23.2	0.92	Light—more	Young more	
Kerr[36]	1943	Boston	500				22.9				
Chesley and Chesley[11]	1943	Jersey City	1,180				23.5				
Averages				2.5	10.8	11.2	24.0	0.86			
Average of individual averages				1.8	10.9	10.7	23.1	0.82			

In some series no dietary control or recommendations have been made, and in others vigorous efforts have been made to hold down the weight gain by restriction of calories, or of salt, or of both.

Table I summarizes some aspects of the literature. All data are given in pounds rather than kilograms since most physicians use the avoirdupois system. Since various authors have approached the problem in different ways, and with different purposes, some violence has occasionally been done in fitting their data to the Procrustean bed which such a summarizing table must be. Thus, for instance, in determining the average weight gain in the last trimester, extrapolations have been made from 12 weeks, and interpolations from 16 weeks. In these calculations, a trimester has been taken as 13.3 weeks. Whenever possible, the gain for the last trimester was computed from the data in Table II. In some of the earlier papers, more than one answer can be derived, because of the varying numbers of patients weighed at different times.

The *average* total gain in normal pregnancy, calculated from the patients' statements as to their prepregnancy weights, is 24.0 pounds (19 publications with 11,960 cases, Table I). The average of the averages is 23.1 pounds, and the range of averages is from 13.3 pounds[28] to 37.4 pounds.[52] Fourteen of the 19 averages fall between 20 and 25 pounds.

The *range* of weight gains to be expected in normal patients is harder to derive, since no publication gives a standard deviation (σ) or a similar statistical factor for variability. The papers of Bingham,[7] of Waters,[63] and of Chesley and Chesley[11] do give the numbers of patients in different weight gain categories, thus permitting the calculation of their standard deviations. These papers are based on large series, totaling half of all reported cases of Table I although Waters unfortunately includes toxemia cases. The standard deviations, as percentages of the respective means (*i.e.*, coefficients of variation) are 45.5, 45.3, and 45.8 for these 3 series. It would, then, seem permissible to assume for the pooled data of Table I, a standard deviation equal at least to 45 per cent of the grand average gain of 24.0 pounds; *i.e.*, $\sigma = 10.8$ pounds.

In a normal frequency curve, the mean $\pm \sigma$ includes 68.26 per cent of all cases, while the mean $\pm 2\sigma$ includes 95.46 per cent of the total. Although the curve derived from Waters' data is slightly skewed, this relation holds within less than 1 per cent.

Applying these relations to the pooled data of Table I, it would appear that about $\frac{2}{3}$ of *normal* patients may be expected to gain between 13 and 35 pounds. Half of the remaining cases, or about $\frac{1}{6}$ of all, may be expected to gain more than 35 pounds. Such gains may horrify the clinician who tries to hold the weight gain below 20, or even below 15 pounds, but in a certain proportion of patients they are normal. Perhaps one might differentiate between weight gain in normal pregnancy and normal or desirable weight gain in pregnancy. This may well be a valid differentiation, since there is evidence that the greater gains are associated with an increasing incidence of certain complications.

Weight Changes in Each Trimester.—It is generally agreed that, on the average, the weight drop which may occur during the phase of anorexia and vomiting and in some patients is just about compensated in the last weeks of the first trimester and by other patients. Thus the net weight change is usually slight—perhaps an average gain of 1 to 3 pounds.[7, 13, 41, 42, 53, 56, 61-63] From the 8 papers (8,877 cases) giving the necessary data, the average gain (weighted by numbers of cases) is 2.5 pounds for the first trimester.

By the end of the first trimester, a fairly steady rate of weight gain begins. One might expect that the rate of gain would be greater in the third trimester, since the absolute growth of the conception product is greatest at this time. Actually the published data are not all in agreement with this expectation, or with each other. In 7 of the 10 relevant papers, the greater gain is found in the second trimester (averages of 5,474 cases). In 3 papers (3,864 cases), the greater average gain is found in the last trimester. The average difference is 0.91 pounds in favor of the second trimester. None of the differences is very marked, being less than 3 pounds in 6 of the 10 papers. The greatest difference[63] is 4 pounds, in favor of the last trimester.

When all of the cases in Table I are pooled, the average gain in the last trimester comes out as 11.2 pounds (18 papers with 12,026 cases), while that for the second trimester is 10.8 pounds (10 papers with 9,338 cases).

One factor which perhaps makes for a greater gain in the second trimester, in some patients, is the replacement of weight lost during the anorexia and vomiting of early pregnancy. However, this is usually compensated in the averages (see above), although in some series it may not have been. Another factor, tending to reduce the average gain in the last trimester, is the prelabor weight loss. Some authors have taken account of this by weighing the patient in early labor. Other authors have computed their weight gains from the weight at the last antepartum visit, which often does not take account of this loss—when it occurs (see below).

Terminal (Prelabor) Weight Loss.—Zangemeister[66] reported that 98 per cent of his patients reached their maximal weight some time before the onset of labor—most commonly on the third day ante partum. There was then a weight loss averaging 2.2 pounds.

This finding has ben confirmed,[35, 47, 50] and denied. Kemper[35] gives an excellent discussion of sources of error in determining this weight loss. Many of the published reports do not conform to the criteria laid down by Kemper. In such papers, many of the weight losses are missed. Some (German papers) do meet Kemper's specifications and yet disagree with Zangemeister. When an average weight curve is drawn, it frequently shows the prelabor weight loss (see, for example, Stander and Pastore[61]). Individual cases are much more variable, and often fail to show the terminal weight drop. Of 15 papers, other than the five mentioned, the weight loss was noted in only from 17 to 40 per cent of 4,026 cases,[4, 5, 13, 14, 20-22, 33, 44, 46, 51,58] and in 63 to 75 per cent of cases.[6, 41, 48] Krüger,[40] and Stander and Pastore[61] remark on its occurrence, but do not give the frequency. The range of the average losses reported is from 0.5 to 2.4 pounds. A few of these papers are included in Table II.

In summary, it would appear that the average weight gains by trimesters are about 2.5, 10.8, and 11.2 pounds, adding up to 24.5 pounds. The average total gain, from Table I, is 24.0 pounds. (The discrepancy is caused by different papers being averaged to get the gains for different periods). The standard deviation is so great that only ⅔ (if that many) of normal patients may be expected to gain 24.0 ± 10.8 pounds. The other ⅓ will show weight changes departing even more radically from the average. A large proportion of patients have a terminal weight loss, but its appearance seems to be inconstant.

The Rate of Weight Gain in the Last Trimester.—The rate of gain toward the end of pregnancy is probably of more significance than is

the total gain for the whole period of gestation, when we come to consider the detection of incipient pre-eclampsia. There are 2 reasons for this: (1) In the great majority of cases, pre-eclampsia appears in the last trimester, and (2) *rapid* weight gains, especially at this time, have usually been interpreted as meaning water retention (edema formation) which is often a harbinger of pre-eclampsia. It is, therefore, important to determine the range and average of normal rates of gain at this time. Some data are given in terms of pounds per week, and some as pounds per month, which may be confusing if not carefully read.

From Table I, the average rate of gain in the last third of pregnancy is 0.86 pounds per week (24 papers with 13,500 cases). The average rates given by 25 different authors range from 0.47 to 1.25 pounds per week, with 64 per cent of the averages falling between 0.7 and 1.0 pounds per week. The average of the averages is 0.82 pounds per week. In many cases, these average rates of weight gain are derived by extrapolation or interpolation from data given for 8 or 12 weeks, or for 16 weeks. However, it would seem that the rate of gain is not constant over this whole period, and slight errors are introduced by the calculations.

TABLE II. THE DECREASING AVERAGE GAIN BY LUNAR MONTHS, AS NORMAL PREGNANCY APPROACHES TERM

AUTHOR	CASES	WEIGHT GAINED, POUNDS LUNAR MONTH				AP WEIGHT LOSS
		7	8	9	10	
Gassner[22]	8 to 89	–	5.3	3.7	3.4	–
Krüger[40]	10 to 57	3.6	3.6	4.6	4.2	In many
Zangemeister[66]	300+	–	3.4	3.4	4.0 (0.4)‡	In 98%
Lorenzen[44]	78	–	–	3.0	3.7	In 17.1%
Kemper[34]	22 to 300	2.4	2.4	3.1	3.1	In 77%
Trillat[62]*	65 to 268	3.4	3.8	3.3	2.7	–
Siddall and Mack[58]	624	4.4	3.9	4.1	3.3	In 24%
Lawson[42]†	220	5.0	4.8	2.8	0.2	–
McIlroy and Rodway[46]	1,000	3.4	3.1	2.9	2.6	In 22%
Frýza[21]	344	3.3	3.3	3.3	3.8	In 32%
Kuo[41]*	200	3.4	3.4	3.1	2.6	In 75%
Stander and Pastore[61]	2,502	4.6	4.0	4.1	2.3 (−0.1)‡	Yes
Average		4.2	3.7	3.6	2.6	

*Interpolated from data for calendar months.
†From graphs.
‡Taking account of prelabor loss.

Table II shows a breakdown of the weight gains by lunar months. Seven of the 12 papers represented therein show the least gain in the last month; the other papers, with the exception of Zangemeister's,[66] Kemper's[34] and Frýza's[21] either do not give data for time periods before the ninth lunar month, or are based on very few observations before that time. The data of Zangemeister and of Kemper, for the tenth month, do not include the prelabor weight loss. When this is considered, the net weight gain becomes least in the tenth month. Frýza's paper was available to me only in abstract, and I do not know whether the gain was computed from the maximal weight or from the final weight. The averages of each column in Table II show a progressive slowing in the rate of gain in the last 4 lunar months. This is particularly interesting since the absolute growth of the conception product is increasingly great during this period.

There are not many quantitative data available as to the variability of rates of gain in late normal pregnancy. Gassner[22] found weight changes varying from 0 to 13.2 pounds in the tenth lunar month (average 3.39 pounds). The standard deviation calculated from his data is 99 per cent of the mean! This signifies that about 34 per cent of the patients gained between average and up to twice the average, while 16 per cent gained even more. Lorenzen[44] remarked that the rate of gain in the last 2 lunar months varied markedly from patient to patient, and in many patients it fluctuated widely from time to time. Trillat[62] found an average rate of gain of 0.82 pounds per week, with a range from minus 0.7 to plus 3.5, in the last trimester of normal pregnancy. Rowe and associates[57] found an average gain of 1.01 pounds per week, with a range from 0 to 2.27 pounds. Harding and Van Wyck[29] considered as normal any gain up to 5 pounds per calendar month (their average?). Gains of more than 8 pounds per month were found in 7.7 per cent of their normal patients. Evans[20] reported an average gain of 2.8 pounds per (calendar?) month, with 33 per cent of normal cases gaining more than 5 pounds, and 21 per cent gaining more than 6 pounds per month in some month (s). The average of *maximal* gains per month, in any of the last 3 or 4 months, was 4.5 pounds. For Dieckmann's 140 normal patients (private communication) the standard deviation is 40 per cent of the mean weekly gain.

Frequency distributions of periodic weight gains in the last 16 weeks of pregnancy are provided in the excellent paper of Siddall and Mack,[58] and also by McIlroy and Rodway.[46] While these data indicate the range of variation in each period (*e.g.*, 24 to 28 weeks, or 32 to 34 weeks, etc.), they are of only limited value because they unfortunately do not show the total number of patients deviating from average of *any* period toward the end of pregnancy. Table III has been derived by recalculation

TABLE III. THE INCREASING VARIABILITY IN RATE OF WEIGHT GAIN AS NORMAL PREGNANCY APPROACHES TERM

Percentages refer to proportions of patients showing weight gains of at least twice average normal for the given period

AUTHOR	CASES	24 TO 28 WEEKS	28 TO 32 WEEKS	32 TO 34 WEEKS	34 TO 36 WEEKS	36 TO 38 WEEKS	38 TO 40 WEEKS	PROPORTION OF PATIENTS SHOWING GAINS OF AT LEAST TWICE AVERAGE, IN AT LEAST ONE PERIOD
Siddall and Mack[58]	460	4.6%	6.1%	11.2%	14.6%	17.5%	35.2%	45.0%
McIlroy and Rodway[46]	1,000	7.3%	8.1%	12.8%	12.2%	20.8%	28.1%	?

of the data in these 2 papers. It will be seen that the rate of gain shows a striking increase in variability as pregnancy approaches term. In Siddall's and Mack's series, 45 per cent of the patients showed at some time a gain of at least twice the average for the period in which it occurred. A comparable datum is not provided by McIlroy and Rodway. (Incidentally, let the reader beware in accepting the general averages in this latter paper. The 704 primiparas and 296 multiparas were analyzed separately, and to obtain the averages for all cases the authors apparently added together the 2 averages and divided by 2. This, of course, does not give the arithmetic mean for all cases.)

In summary, the rate of weight gain in the last trimester is markedly variable, and the variability increases as pregnancy approaches term.

Factors Affecting Weight Gain During Pregnancy.—The factors which will be considered are summarized in Table I.

1. *Initial Body Weight.*—In 9 papers (3,898 cases) it was found that heavier women gain more on the average, than the lighter ones. Four papers, with 4,630 cases, came to the opposite conclusion, while in 3 papers (945 cases) it is stated that there is no significant difference. Gassner[22] concluded that the gain was roughly in proportion to the initial body weight, and this conclusion was accepted by the subsequent workers in Germany. Wodon[65] carried the concept further in setting the normal average gain at 20 per cent of the initial weight, which figure was also accepted by Pugliatti.[55] Stander and Pastore[61] set the normal average gain at 24.1 per cent of the weight at 6 weeks (essentially equal to the initial weight). For an already overweight woman, this seems to be rather extravagant. Not many obstetricians would accept with equanimity gains averaging 50 pounds in their 200-pound patients. (This is not to deny the tendency to such gains.)

2. *Age.*—In 8 papers (5,885 cases) it is concluded that young women gain more than old. Only 1 paper (Krüger,[40] 57 patients) comes to the opposite conclusion, that the older patients gain more. Bray[8] (69 cases) found no difference in the 3 age groups into which he divided his cases.

3. *Parity.*—Twenty-one papers reach a conclusion as to the relation between parity and weight gain. In 8, with 5,799 cases, it is stated that there is no significant difference between primiparas and multiparas. Another 8 papers (1,249 cases) find a greater gain in multiparas, while 5 papers (1,418 cases) report a greater gain in primiparas. Where differences are found, they usually are not very great, and are probably not truly significant. This is well shown in the paper of McIlroy and Rodway; the multiparas had a somewhat greater average weight gain, but when the frequency distribution curves are plotted for different weight gain classes, one can see at a glance that the primiparas and multiparas do not differ.

Twin Pregnancy.—Except for a few scattered cases, the only available data on the weight gain in normal twin pregnancy are supplied by Stander and Pastore.[61] In 95 normal cases, they found an average gain of *less* than in single pregnancy, *i.e.*, 21.1 per cent of the weight at 6 weeks as compared with the 24.1 per cent gain in single pregnancy.

Weight Changes at Delivery and in the Puerperium (Normal Cases)

The weight changes occurring in normal patients at delivery and in the puerperium are summarized in Table IV. Gassner's[22] series included some edematous patients, and for that reason his data for puerperal weight loss are higher than would be the case for strictly normal subjects. Leaving his figures out of consideration for the moment, the average total weights lost from just ante partum to about the tenth day post partum are in fairly good agreement as among the 12 published papers. The average weight loss for all patients (roughly 4,000) is 17.9 pounds, with a range of published averages running from 15.1 to 21.7 pounds (Gassner's average: 25.5 pounds). The average of the averages is 18.7 pounds (or omitting Gassner's, 18.1 pounds).

The data of Table IV cover only the first 6 to 14 days of the puerperium. There are not many data available which bear on the weight changes occurring in the later puerperium. Gassner weighed 10 of his patients at 3 to 6 weeks after delivery, and found that all had gained weight since discharge from the hospital. However, in his day, the management of the puerperium involved a low caloric intake, which, together with the inclusion of edematous patients, perhaps contributes to his large weight losses (av. 10.1 pounds) of the first week after delivery. Stander and Pastore[61] weighed an unspecified proportion of their 2,502 normal patients at 6 weeks post partum, and found an average loss of 1.5 pounds occurring between the tenth day and sixth week after delivery. The average weight at the sixth week post partum was somewhat greater than the average prepregnancy weight; for primiparas the difference was 4.8 pounds, and for multiparas 3.7 pounds. (Because of the different numbers of patients weighed at various times, the figures do not "add up." The gain to maximal weight averaged 30.7 pounds. The losses were: prelabor 2.42, delivery 11.75, early puerperal 5.06, and late puerperal 1.50 pounds. These losses total 20.7 pounds, or 10 pounds less than the weight gained during pregnancy, leaving 5 to 6 pounds unaccounted for in the averages.) Waters[63] gives no detailed data, but states that "Roughly, in the latter group (tissue gainers as differentiated from water gainers, L. C. C.) it may be said that patients will retain beyond six weeks 60 to 80 per cent of all weight gained in excess of 22 pounds," and "postpartum weight loss is within 5 pounds of the total gain for all patients who gained the average poundage."

There is not much which can be said about the variability of the weight lost at delivery and in the early puerperium, because very few relevant data have been published. Apparently, however, this weight loss varies within a considerably narrower range than does the gain during pregnancy. For instance, the standard deviation, calculated from Gassner's data on weight loss, is only 24.2 per cent of the mean. This may be compared with σ for his data on weight change in the tenth month ($\sigma = 99$ per cent of the mean). Gassner's antepartum gains, and puerperal losses probably vary more than would be found in strictly normal patients, since he included some edematous cases. The standard deviations for Baumm's[2] data on weight losses at delivery and in the following 6 days are 15.4 and 34.6 per cent of the respective means.

The delivery plus early puerperal weight losses in normal twin pregnancy are considerably greater than can be accounted for by adding the weight of the second child to the losses sustained after single pregnancy. The average loss is 26.8 pounds for the 172 cases in Table IV (excluding Baumm's[2] obviously abnormal case, and those of Mauks[48] whose number is uncertain). Stander and Pastore[61] found that, as compared with single pregnancy, twin pregnancy showed a lesser gain ante partum, and a greater loss both at delivery and in the early puerperium. In the last 5 weeks of the puerperium, there was a gain in weight as contrasted with the further loss sustained by women having single pregnancies.

In summary, the delivery plus puerperal weight losses average about 18 pounds. Many patients fail to return to their pre-pregnancy weights, and the greater the gain during pregnancy (excluding water-gainers), the greater is the net gain left to the maternal organism. This constitutes a good reason for limiting the weight gain in pregnancy to about 20 pounds, as many a husband who married a slip of a girl could testify.

TABLE IV. THE AVERAGE WEIGHT LOSSES SUSTAINED AT DELIVERY AND IN THE EARLY PUERPERIUM: NONTOXIC CASES

AUTHOR	YEAR	LOCALITY	CASES	SINGLE PREGNANCY			TWIN PREGNANCY			
				POUNDS LOST AT DELIVERY	POUNDS LOST IN EARLY PUERPERIUM	DELIVERY PLUS EARLY PUERPERAL LOSSES, POUNDS	CASES	POUNDS LOST AT DELIVERY	POUNDS LOST IN EARLY PUERPERIUM	DELIVERY PLUS EARLY PUERPERAL LOSSES, POUNDS
Gassner[22]	1862	Munich	189 to 282	14.44	10.06	25.5	2	26.00	12.37	38.4
Kleinwächter[38]	1874	Prague	6		6.19					
Klemmer[39]	1876	Dresden	24		1.70					
Solovjev[60a]	1879	Kazan	40	16.5	1.70	18.2				
Góth[23]	1881	Kolozsvar	10+80	14.5	7.70					
Baumm[2]	1887	Munich	60	13.73	8.01	21.7	1	23.22	28.85	52.1
Heil[31]	1896	Heidelberg	100		5.06		1		17.43	
Krüger[40]	1909	Halle	49			18.6				
Zangemeister[66]	1916	Marburg	77	13.05	3.54	16.6				
Kemper[34]	1924	Marburg	339	12.32	2.76	15.1	11	20.95	4.11	25.1
Kerwin[37]	1926	St. Louis	152			16.3				
Plass and Yoakam[52]	1929	Iowa City	48			19.8				
Rowe, Gallivan and Matthews[57]	1931	Boston	77			19.6				
McIlroy and Rodway[46]	1937	London	710			20.5*				
Bray[8]	1938	Duluth	64		6.24					
Mauks[48]	1939	Budapest	208			17.6	?			26.2
Guttmacher[25]	1939	Baltimore					64			26.2
Bertini[5]	1939	Turin	64			19.3				
Stander and Pastore[61]	1940	New York	†	11.75	5.06	16.8	95	17.45	9.75	27.2
Chesley and Boog[76]	1943	Jersey City	16 to 30	10.28	5.46	15.8				
Averages				12.0	5.2	17.9		18.0	9.5	26.8
Average of averages				12.6	5.4	18.7		21.9	14.5	32.5

*Weight lost from just ante partum to 6 weeks post partum.

†Unspecified proportion of 2,502 patients. In calculating the averages, 2,400 were assumed for the delivery losses, and 2,000 for the early puerperal losses.

Relation of Weight Gain to Toxemia

Insofar as possible, "toxemia" will refer to pre-eclampsia and eclampsia, as defined by the American Committee on Maternal Welfare. Unfortunately, some of the papers do not differentiate between the different classes of toxemias.

Gassner,[22] in 1862, correlated excessive puerperal weight losses with diuresis and the discharge of edema fluid which had been accumulated during pregnancy. However, Zangemeister[66] in 1916, was the first to emphasize that edema formation and incipient toxemia could be detected by periodic weighings of pregnant women.

Some writers have not made a distinction between water gain and "stereoplasmic gain" (Waters' term), and have regarded any excessive weight increase as a harbinger of toxemia. Indeed, it has been conceived that overloading the maternal organism with stored fat and protein may of itself lead to toxemia. However, the consensus of opinion today is that weight gains significant for the development of toxemia represent water retention. While weight taking is obviously nonspecific, it is of some value in that rapid and excessive gains in weight have been interpreted as pointing to water accumulation. As mentioned before, the rate of gain in the last trimester is probably of more significance than is the total gain in pregnancy.

Total Weight Change in Toxemia.—Table V shows 7 publications in which the average total weight gains are compared for normal and for toxic pregnancies. Randall,[56] with only 12 cases of toxemia, found the average normal weight gain to be doubled in the toxemia patients. At the other extreme, Stander and Pastore[61] report that the average total weight gain in their 2,502 normal patients was essentially the same as in their 177 cases of mild and severe pre-eclampsia (mild pre-eclampsia taken as the equivalent of their "low reserve kidney"). In their 30 cases of eclampsia, the average gain was slightly greater (being about 2.5 pounds above average normal), but most of the extra gain occurred in the last week or two. Their data for total gains, in percentages of the weight at 6 weeks, are: normals 24.1, "low reserve kidney" 24.46, pre-eclampsia (severe, L. C. C.) 25.15, and eclampsia 26.15. In the other 5 publications, the average total gain in toxemic patients ranges from 2 to more than 6 pounds above the respective averages for normal patients. If one were able to plot frequency distribution curves for total weight gains in normal and in toxemic patients, it would seem that most of the toxemic patients would fall within the normal range, and nearly half would have less than average "normal" gains.

Another approach to the question is summarized in Table VI. As the total weight gain becomes greater, the incidence of toxemia increases. Bingham[7] and Chesley and Chesley[11] are the only authors to give data for the numbers of normal and of toxemic patients in each weight gain category, and they did find that the incidence of toxemia mounted as the weight gain increased. However, 72 per cent of the toxemia cases in each series had weight gains of less than 30 pounds. About 88 per cent of the patients, in each series, who gained more than 30 pounds did not have toxemia.

Dieckmann and Brown[17] found that 57 per cent of about 570 pre-eclamptics gained less than 22 pounds, and 71 per cent less than 26.5 pounds.

TABLE V. COMPARISON OF NORMAL AND TOXIC PREGNANCIES IN RESPECT TO TOTAL WEIGHT GAIN AND RATE OF GAIN IN LAST TRIMESTER

AUTHOR	NORMAL PREGNANCY		TOXIC PREGNANCY		INCIDENCE OF TOXEMIA PER CENT		INCIDENCE RATIO	ABNORMAL GAIN BEFORE OTHER SIGNS OF TOXEMIA	CASES	
	TOTAL GAIN POUNDS	POUNDS/ WEEK IN LAST TRIMESTER	TOTAL GAIN POUNDS	POUNDS/ WEEK IN LAST TRIMESTER	IN NORMAL WEIGHT GAIN	IN ABNORMAL WEIGHT GAIN	NORMAL GAIN / ABNORMAL GAIN		NORMAL	TOXEMIA
Randall[56]	22.5	0.85	44.5	3.18				Yes	300	12
Bingham[7]	19.9	0.53	25.6		1.3	6.4	1:5	Yes	1,288	50
Siddal and Mack[59]		0.96		1.06		5.9	1:1 (about)	In 37 per cent	624	100
Cummings[13]	24.1	0.79	>30.0			48.0		Yes	937	63
Harding and Van Wyck[29]		1.25			0.0			Yes	719	7
Wodon[65]		1.10*		>1.10	7.9	76.6	1:10	Yes	311	89
Evans[20]		0.63		1.10	0.6	49.0	1:82	In 65 per cent	159	52
McIlroy and Rodway[46]		0.74		1.06				Yes	1,000	75
Pugliatti[55]	22.0	?		Doubled					200	?
Mauks[48]	22.0	0.70	27.1	1.00		30.0		Yes	208	168
Bertini[5]	21.8†P	1.08P	26.3†P					Yes	228	14
	27.7†M	0.73M	36.7†M							
Stander and Pastore[61]	24.1%	0.75%	24.8%	0.84%					2,502	207
Chesley and Chesley[11]	23.5		25.7						1,180	98

*Upper normal.

†Gain in last 6 months. While Bertini's multiparas had a greater 6-month gain than his primiparas, the latter gained faster in the last trimester.

P = Primiparas; M = multiparas.

TABLE VI. THE INCREASING INCIDENCE OF TOXEMIA CORRELATED WITH HIGHER TOTAL WEIGHT GAINS

AUTHOR	CASES	TOTAL WEIGHT GAIN IN POUNDS						
		0 TO 10	11 TO 20	21 TO 25	26 TO 30	31 TO 35	36 TO 40	41+
Bingham[7]	1,338	0.7%	1.5%	5.3%		10.6%		
Cummings[13]	1,000					48.0%*		
Waters[63]	1,459			3.5	5.5	11.8		
Chesley and Chesley[11]	1,278	6.2%	9.3%	9.8%		12.8%		13.0%

*"Showed signs of toxemia or actually developed it." Only 22 patients of the 1,000 had "large amounts of albumin"; all of these had gained more than 30 pounds. These 22 patients represent 16.8 per cent of the 131 having such gains.

Briefly, the total weight gain in pregnancy does not seem to be of much value in detecting incipient toxemia. Many, perhaps most patients who develop toxemia have had normal total weight gains. Relatively few patients with higher weight gains do become toxemic.

Rate of Gain in Last Trimester.—All of the 8 relevant papers represented in Table V agree that toxemic patients show an augmented rate of weight gain in the last trimester. The differences between average rates of gain in normal and in toxemic patients are often not well marked. However, this may be attributable to the fact that the average rate of gain is calculated for the whole trimester, and sudden spurts occurring in one or two weekly periods are obscured. Nearly all writers are agreed that rapid weight gain frequently precedes hypertension and other signs of toxemia, often by weeks. In other cases the rapid gain coincides with the appearance of hypertension, and sometimes it does not occur at all.

It seems well established that, on the average, pretoxic patients gain weight more rapidly than the average rate for normal patients. However, there is a serious paucity of data bearing on the questions as to what is the normal range of gain, how many patients develop toxemia without abnormally rapid gains, and how many patients have abnormal rates of gain and do not develop toxemia. Most of the conclusions have been drawn from insufficiently worked data.

Siddall and Mack[59] have made a critical analysis of their data, and concluded that "the occurrence of excessive weight gains in pregnancy would appear to be of doubtful significance in predicting impending toxemia." They found that 61 per cent of their 100 toxemia cases had weight gains of at least twice average at one or more periods after the seventh lunar month. The other 39 per cent "had no excessive gain at any time," and in the last four months gained an average of only 11.6 pounds as compared with 15.7 pounds in normal patients. Of the 61 patients who did have excessive rates of gain, the rapid gain preceded hypertension in 37 cases. "Since excessive weight increase preceded other signs in 37 per cent of toxemias, it might seem of real value in discovering the disease in its incipiency." But, as was pointed out in the section on rate of gain in normal pregnancy, these workers found that 45 per cent of normal patients also showed comparably excessive gains at one or more periods in the last 4 months. "Consequently, our figures indicate that acceptance of excessive gain as reliable evidence of incipient toxemia necessities subjecting approximately one-half of all

pregnant women to treatment.'' Table III offers perhaps the only escape from these conclusions. As normal pregnancy approaches term, the variability of weight gain increases markedly, and in the last 2 weeks, 35.2 per cent of Siddall's and Mack's patients showed gains of at least twice the average for this period. If a large proportion of the 45 per cent showing twice average gains at any time, had the abnormal gains only in the last 2 weeks, then the gains occurring earlier in pretoxic patients would have added significance. It is hardly fair to expect excessive gain to predict future toxemia if that gain occurs when delivery is imminent. Unfortunately, one cannot determine this point from the published data.

The two papers in which excessive rates of gain have been alleged to be most closely correlated with the development of toxemia are those of Wodon[65] and of Evans.[20] In discussing Evans' paper, Siddall and Mack[59] write ''conclusions were based on the records of only 211 patients (apparently a series of consecutive cases) of whom the surprising number of 52 were classified as toxemia.'' Wodon's series is equally astonishing—89 toxemias in 400 patients. The toxemia incidences would be: Evans, 24.6 per cent and Wodon, 22.3 per cent. Siddall and Mack question the validity of many of the diagnoses, and it seems to me justifiably so. Accepting Evans' diagnoses, we find that the average monthly gain in the toxemias was 4.3 pounds, as compared with 2.8 pounds in normal patients. A maximal gain of 5 pounds in any month almost made a separation of normal from toxic patients. Those women who never exceeded this gain had a toxemia incidence of 0.6 per cent, and only 2 per cent of all toxemias occurred in this class. In the women gaining more than 5 pounds in any month, the toxemia incidence was 49 per cent, and 98 per cent of the toxemias were associated with such gains. Exactly ⅓ of the normal patients did have maximal gains of more than 5 pounds in some month.

Wodon[65] found a toxemia incidence of 7.9 per cent among 306 patients whose weekly weight gain never exceeded 1.1 pounds. In the 94 patients who did show greater gains, the incidence of toxemia was 76.6 per cent. Omitting patients whose only toxic sign was a mild elevation in blood pressure, the incidences of toxemia would be 2.3 and 20.2 per cent in the respective groups. The ratio of toxemia incidences is roughly 1:10, either with or without the questionable cases.

Harding and Van Wyck,[29] in a series of 726 unselected private patients, found that all of their toxemias (excluding one case of ''chronic nephritis'') had shown monthly gains of 8 pounds or more. No further data are given as to the distribution of weight gains. Mauks[48] states that toxemia developed in 30 per cent of his patients who gained more than 4.4 pounds per calendar month. His average monthly gains were: in normals 3.1 pounds, in mild toxemia 3.7 pounds, and in severe toxemia 5.5 pounds. Dieckmann and Brown[17] found that 74 per cent of their severe pre-eclamptics gained more than 1.3 pounds per week, and 24 per cent gained more than 2.2 pounds per week. Conversely, 76 per cent gained less than 2.2 pounds per week, and 26 per cent gained less than 1.3 pounds per week. (These are apparently average figures for the whole period of observation. Maximal figures are not given, either for normals or for toxemias.) McIlroy and Rodway[46] do not give the variations in rate of gain occurring at any time, but apparently doubled gains were 3 to 5 times more frequent in toxemias than in normals.

In summary, many pretoxic patients gain weight rapidly. The absence of such gain is no insurance against the development of preeclampsia, and a large number of patients who will not become toxemic will scare the physician with definitely "abnormal" rates of gain. Pooling the data of Siddall and Mack,[59] of McIlroy and Rodway,[46] and of Evans,[20] it would seem that about 54 per cent of toxemia patients will show, at some time, a weight gain of at least twice the average for that period. Nearly 40 per cent of normal patients will show similar gains (figures approximate).

Delivery and Early Puerperal Weight Losses (Toxemias)

Zangemeister[67] found the total weight lost from just ante partum to the tenth day post partum to average 27.1 pounds in 8 patients with "hydrops gravidarum." The average loss in his normal patients was 16.6 pounds. Bertini[5] reports the weight loss (to the seventh day) in 8 toxemias as averaging 24.9 pounds; his normal patients lost an average of 19.3 pounds. Stander and Pastore[61] give figures for about 200 toxemias, whose weight loss (to the tenth day) averaged 20.6 pounds as compared with a loss of 16.8 pounds in their normals.

Presumably this excessive loss, which occurs so rapidly after delivery, represents the discharge of edema fluid.

What Constitutes the Maternal Weight Gain?

The combined data of Baumm,[2] Gassner,[22] Kemper[34] and Lehn[43] show an average weight of baby + after birth + amniotic fluid in 958 cases amounting to an average of 11.18 pounds. This is a little less than half of the total average gain shown by the mother. In about 10 per cent of 6,046 term pregnancies[7, 11, 41, 63] this "reproductive weight" is greater than the total weight gain shown by the mothers, some of whom actually have weight losses. In such cases, of course, there has been a net loss to the maternal organism. However, in the majority of cases there accrue to the maternal tissues considerable gains in weight; in perhaps a fifth of cases this net gain, exclusive of the conception product, exceeds 20 pounds. On the average, this net gain to the maternal organism amounts to about 10 per cent of the prepregnancy weight (Net gain = total gain of 24 pounds minus 11.2 pounds of conception product = 12.8 pounds. Average prepregnancy weight = 128 pounds, according to Stander and Pastore.[61])

The few studies made with other pregnant animals, summarized in Table VII, indicate net gains to the mother amounting to an average of 11.6 per cent above the expected weight. The "expected weight" is the weight of the unbred controls which were often litter mates, or at least were animals of the same age and initial weight at the time of breeding the experimental animals. Edlefsen's[19] work on guinea pigs is omitted, because he used immature animals, and his only controls were males.

There are certain necessary changes in the maternal organism incident to pregnancy. First, there is the growth of the uterus and its adnexa. According to Reynolds,[124] the uterine mass increases from about 30 to 60 grams to 1,000 to 1,400 Gm., an increase of 2.07 to 3.02 pounds, or about 2.5 pounds as an average figure. Second, there is the enlargement of the breasts which varies greatly. Evans[20] estimates this factor at 2 to 4 pounds.

TABLE VII. THE NET GAIN IN WEIGHT ACCRUING TO MATERNAL TISSUES DURING PREGNANCY IN ANIMALS OTHER THAN WOMAN

AUTHOR	ANIMAL USED	NO. OF ANIMALS	PERCENTAGE GAIN ACCRUING TO MATERNAL TISSUES DURING PREGNANCY	REMARKS
Minot[49]	Guinea pigs	66	15 per cent	Rapid loss of weight in first 5 days postpartum
Herring[32]	Rats	9	No gain	
Hartwell[30]	Rats	6 in 40 pregnancies	13 per cent	Initial weight assumed to be 200 Gm.
Hain[26]	Rats	16	12 to 15 per cent	
Abramson[1]	Rats	44	6 per cent	
Bruhl and Vogel[9]	Mice	4	16 per cent	Immature mice omitted (gain more)
Poo, Lew and Addis[54]	Rats	20	12 per cent	Up to eighteenth day of 23-day pregnancy
Totals and mean		199	11.6 per cent	

Adding these components to the weight of the conception product, we can account for about 17 pounds of the total gain shown by the pregnant woman. This leaves an average of about 7 pounds, and in many cases much more, yet to be explained.

Opinion has varied greatly as to what constitutes this additional maternal gain, and as to the proportionate parts contributed by the different factors which have been recognized. In the present review, the following will be considered: 1. Protein (nitrogen), and 2. water, with electrolytes. Fat will not be discussed for want of quantitative data. Obviously, some patients gain a great deal of fat, and others very little. Because of the many facets of the problem, complete reviews of the relevant literature will not be attempted. References will be made only to summarizing papers, or to papers most germane to the topic in hand.

1. *Protein (Nitrogen) Retention.*—Hunscher and associates[106] in 1933 reviewed the literature on nitrogen retention in pregnancy. From 945 daily N balances, they calculated that the average retention was 2.28 grams per day over the last 8 lunar months. This would give a total N storage of 511 grams. From the available estimates in the literature, they set the N requirements as follows: fetus 70 Gm., placenta, cord and blood 18.0 Gm., amniotic fluid 0.86 Gm., breasts 17 Gm., and uterus 38 Gm.; total about 145 Gm. This would leave 366 grams for the maternal organism (exclusive of the reproductive system). In a later paper, Hunscher and others[107] followed a multipara continuously during the last 145 days of pregnancy, and found that she stored 446.2 Gm. of N. It was estimated that 300 Gm. of this was in the maternal tissues outside the reproductive system. Seegars[128] found a comparable N storage in a young primipara. Thompson and Pommerenke[137] found a far lesser degree of N storage in 2 women studied at different times in pregnancy. They seem inclined to accept the results in the literature

as being more typical than their own cases. Freyberg, Reekie and Folsome[96] followed a young primipara over the last 62 days of pregnancy, and found an N retention averaging only 0.82 Gm. per day in contrast to the average of 2.28 Gm. from Hunscher's summary of the literature. Oberst and Plass[120] found N retentions in 5 young primiparas which averaged close to the figure of 2.28; retention was somewhat greater in the fifth and sixth lunar months than in later pregnancy. Coons and associates[82] found comparable N retentions in 6 patients.

It would seem, then, that about a pound of nitrogen is retained during pregnancy. Presumably this is stored as protein, which would weigh about 6¼ pounds. If this protein were used in the formation of new tissue, with the usual proportion of water (as in muscle tissue for instance), the expected weight increment attributable to N storage alone would be 30 to 35 pounds. Since such weight gains are not the rule, the protein (if such be the storage form) must be packed away somewhere in concentrated form.

In looking for the site of stored protein, one thinks at once of the liver. A fairly extensive search of the literature on human liver weights has turned up just one bald statement which almost seems irrelevant in the paper in which it occurs. Bean and Baker[71] write "The liver in pregnant women is considerably larger than the average of the normal liver weight." They make no other mention of pregnancy, and no figures are given for livers from pregnant women. However, there are several papers describing changes in organ weights incident to pregnancy in rats and mice. Herring[32] found the liver weight to increase 27.5 per cent in pregnant rats. MacKay[45] found the increase to be 20 per cent; Abramson[1] about 13 per cent. Brühl and Vogel[9] found the liver weight in 7 white mice to increase 39 per cent. Liesenfeld, Dahmen and Junkersdorf[115] found only slight increases in liver weight in 2 pregnant dogs, and a decrease in their third dog. Poo, Lew and Addis,[54] in 20 rats, found that by the eighteenth day of pregnancy the liver had increased about 40 per cent in weight as compared with the controls.

Poo, Lew and Addis[54] analyzed the various organs of their rats for protein content. They found a 34 per cent increase in the total amount of protein in the liver. There was also a 25 per cent increase in the protein content of the alimentary tract. The protein increment in the carcass was only 2 to 3 per cent. Of the total protein gained, 36 per cent was in the liver and alimentary tract, 36 per cent in the uterus, and 29 per cent in the carcass. The actual concentration of protein was decreased, during pregnancy, in the liver, blood, kidney and heart. That is, stored protein apparently was associated with even more than the usual proportion of water. How far these figures are applicable to human beings is questionable. Certainly the uterine growth in rats is out of proportion to that in women.

Briefly, then, it seems that at least 6 pounds of the average maternal gain during human pregnancy can be attributed to protein storage. Of this, perhaps two-thirds is to be found outside of the reproductive system. If the protein be associated with the usual proportions of water, as it seems to be in the rat, the storage in human maternal tissues would call for unreasonable weight gains of the order of 20 pounds attributable to this factor alone.

2. *Water Retention in Normal Pregnancy.*—It is generally recognized that normal pregnancy is accompanied by some degree of water reten-

tion. Since the noncolloidal osmotic relations do not seem to be significantly disturbed in pregnancy, there must be a proportional retention of electrolytes. The clinical observations indicating that water retention does occur during pregnancy are: 1. The marked postpartum diuresis (see Crabtree[84]); 2. the simultaneous rapid weight loss in the early puerperium (Table IV); and 3. the atonic and flaccid condition of the tissues after the diuresis (discharge of edema fluid). A variation on the third observation is the demonstration of a shrinkage in the circumferences of the arms, legs and neck in the first few days after delivery, occurring in 95 per cent of cases (Fink,[95] Gueissaz[100]).

Physiologic measurements pointing to water retention are: 1. The increase in venous pressure in the legs; 2. the decrease in colloid osmotic pressure of the plasma; and 3. the positive sodium balance throughout most of pregnancy. 4. Still another factor contributing to water retention during pregnancy is the presence of huge quantities of the steroidal sex hormones, which perhaps are responsible for the sodium retention.

In determining the distribution of the retained water, a considerable quantity can be allocated to the blood itself. Dieckmann and Wegner[89] (see for review of earlier work), Thomson and associates,[139] and Albers[69] have found that the total blood volume increases markedly during pregnancy. These increases were found by the authors cited to be, at term, 20 per cent, 30 per cent and 29 per cent respectively. All found that the plasma volume increased more than the cell volume. Oberst and Plass[121] have shown that the water content of both plasma and cells is increased in pregnancy. The average water gain represented in the increased blood volume might be calculated as follows. The average woman's nonpregnant weight is close to 128 pounds (Stander and Pastore[61]), and she gains about 24 pounds in pregnancy (Table I). The data of Thomson and associates[139] show a blood volume of 30.1 ml. per pound at 30 days or more post partum (checking closely with other measurements of blood volume in nonpregnant women), and a volume of 35.1 ml. per pound in the last month of pregnancy. The difference in total blood volumes would be about 1,490 ml., or 3.45 pounds (specific gravity of whole blood as 1.055). Oberst and Plass[121] give the average water content of whole blood as 811 Gm. per kilo of blood for nonpregnant women, and 827 Gm. per kilo in late normal pregnancy. The total gain in blood water then would be about 1,300 Gm., or 2.9 pounds.

The volume of the interstitial water depends upon at least 3 major factors, viz.: 1. The effective intracapillary hydrostatic pressure which impels filtration from the vascular bed; 2. the effective colloidal osmotic (oncotic) pressure of the plasma, which limits filtration and effects reabsorption of filtered water; and 3. the rate of lymphatic drainage. Also changes in capillary permeability perhaps may be operative at times. ("Effective pressures" refer to the differentials between the intra- and extra-vascular forces). Normally, these 3 factors are nicely balanced, and the interstitial fluid volume is thereby maintained with a fair degree of constancy. If the volume is to remain constant, a disturbance in one of these factors must be compensated by adjustments in the others.

In pregnancy there is an increase in capillary pressure in the legs, and the oncotic pressure is diminished. Both of these factors make for an increase in the interstitial water volume. The extent to which lymphatic drainage undergoes a compensatory increase is unknown, at least to me.

Measurements of capillary pressure have been attempted by various techniques but most of the data are unsatisfactory. The problem has therefore been approached by determinations of venous pressure. McLennan[116] has recently reviewed the literature, and contributed a superb study made on 255 of his own subjects. He concludes that the antecubital venous pressures are not increased in normal pregnancy, agreeing therein with 8 of the 16 earlier reports which he reviewed. The femoral venous pressure rose from 91 mm. of water in early pregnancy to a peak value, at term, of about 244 mm. of water (average of 42 patients). All 7 previous reports agreed that the femoral venous pressure was increased in pregnancy. The increased femoral pressure, of course, would be considerably augmented by the assumption of the upright position—McLennan's measurements were made with the subjects supine. Róna[125] determined the saphenous pressure in pregnancy with patients standing. The average pressure at the level of the venepuncture was 938 mm. H_2O, and ranged from 792 to 1,230. These markedly elevated femoral venous pressures must be reflected in the capillaries of the legs. Since this hydrostatic pressure approaches, or on standing exceeds, the oncotic pressure (see Table VIII), there must be an increased filtration and a diminished capillary reabsorption in the legs, thus predisposing to the accumulation of interstitial fluid. The transudation is limited, of course, by the increasing extravascular tissue pressure.[113] (Even in nonpregnant individuals, prolonged standing will result in a demonstrable increase in leg volume, though not visible edema, and concentration of the blood.[138]) Since the legs constitute about 37 per cent of the body weight,[141] considerable volumes of water may be thus retained. During recumbency, some or all of this accumulated water may be mobilized and excreted, thus accounting for the observation that late in pregnancy the night urine volume approaches or exceeds the day volume.[136]

As Table VIII shows, the colloidal osmotic pressure of the plasma is diminished by about 20 per cent during pregnancy. This is attributable to the characteristic drop in serum proteins, amounting to about 1 gram per 100 ml. of serum.[88] As Dieckmann[88] has pointed out, this diminution in proteins and oncotic pressure is not sufficient to account for the palpable edema of either normal or toxic pregnancy (Strauss,[130] however, has attributed the edema of toxemia to decreased oncotic pressure along with other factors). While the changes in proteins occurring in normal pregnancy are not great enough to cause edema, they may well lead to some degree of water retention which would not show up as visible edema. The statement is commonly made that the body can retain water up to 10 per cent of its weight before edema becomes evident. I have not been able to find the original work upon which this statement is based. However, Drury and Jones[92] have shown that fluid accumulation in the legs must increase by 8 per cent before edema becomes evident. Weech, Snelling and Goettsch[143] produced edema in dogs by plasmapheresis and by protein restriction. Their results ". . . suggest an equilibrium between plasma proteins and the volume of fluid in the interstitial spaces. The equilibrium seems to be maintained throughout the entire range of protein variation in such a way that every slight protein decline leads to a correspondingly slight increase in interstitial fluid."

Goudsmit and Louis,[99] in a quantitative study, found that a decrease in serum proteins of 1 gram per 100 ml. will result in an increase in

TABLE VIII. ONCOTIC PRESSURE OF PLASMA OR SERUM IN PREGNANCY

Drinker and Field, in review of literature, found an average of 367 mm. H_2O for 361 nonpregnant normals. Range of averages 286 to 431

AUTHOR	NORMAL PREGNANCY WITHOUT EDEMA						NORMAL PREGNANCY, LATE, WITH EDEMA			PRE-ECLAMPSIA			ECLAMPSIA		
	EARLY PREGNANCY			LAST TRIMESTER											
	CASES	MEAN	RANGE	CASES	MEAN	RANGE	CASES	MEAN	RANGE	CASES	MEAN	RANGE	CASES	MEAN	RANGE
Runge and Kessler[127]	18	391	317 to 455	26	323	243 to 350									
Kaboth[108]				14	316	253 to 362				7	263	180 to 342	7	231	188 to 277
Kylin[112]										7	228	143 to 315	2	220	196 and 245
Baráth and von Magyary[70]				3	317	314 to 322	4	318	311 to 328						
Orrù[122]	14	348	303 to 405	42	297	261 to 392	14	293	273 to 336	4	284	272 to 296	5†	214	160 to 272
Martines and De Lauretis[118]	14	259	170 to 376	56‡	245	138 to 394				2	236	230 to 243	5	284	212 to 346
Dieckmann and Kramer[88]				15	287	226 to 381				22	255	210 to 301			
Totals and averages	46	338	170 to 455	156	284	138 to 394	18	298	273 to 336	42	254	143 to 342	19	239	160 to 346

*Omitting 3 extremes range would be 275 to 332.
†One patient counted twice.
‡Some probably had edema.

TABLE IX. SODIUM RETENTION DURING NORMAL PREGNANCY

The last column is calculated from the assumption that all sodium is held extracellularly, is osmotically active, and that its concentration in extracellular water is 336 mg. per 100 ml.

AUTHOR	CASES	PERIOD IN PREGNANCY	MEAN DAILY RETENTION OF Na, GM.	TOTAL RETENTION, GRAMS PER WEEK	CALCULATED GAIN IN EXTRACELLULAR H_2O LITERS PER WEEK
Coons and associates[81]	5	Near end	1.26	8.81	2.620
Hummel and associates[105]	1	Last 21 weeks	0.56	3.92	1.167
Freyberg and associates[96]	1	Last 70 days	0.231	1.61	0.473
Thompson and Pommerenke[137]	1	In fourth and eighth months	0.44 0.267	3.08 1.87	0.917 0.557
Taylor and associates[132]	4	Last 13 to 23 days	0.440	3.08	0.917
Taylor and associates[133]	3	First 10 days p.p.	-0.489	Total loss, first 10 days p.p. 4.89	Total loss, first 10 days p.p. 1.455

interstitial water amounting to 3.8 ± 0.8 per cent of the body weight. In our average patient who has gained from an initial 128 up to 152 pounds in pregnancy, this factor would, then, account for a water gain of about 5.8 pounds.

The sodium retention of pregnancy is summarized in Table IX. In the last column of the table is shown the volume of extracellular water gain per week to be expected if all of the sodium is held extracellularly in osmotically active form, and if blood and tissue fluids are not to show any significant increase in sodium concentration (see papers of De Snoo,[86] Zangemeister,[67] Rossenbeck,[126] and of Taylor, Warner and Welsh[133] for review of literature, indicating that sodium concentrations are essentially unchanged in pregnancy). Since these calculated volumes of water gain are unreasonably high, some of the sodium must be stored in an osmotically inactive form. Perhaps this osmotically inactive sodium is bound to proteins, or stored in the bones. Rossenbeck[126] found from direct analysis of various tissues that the sodium content is increased in normal pregnancy, and markedly increased in eclampsia. In normal pregnancy, he calculates that the excess muscle sodium amounts to about 3 grams. This is only a fraction of the total amount stored during pregnancy.

Taylor, Warner and Welsh[133] provide a review of the effect of the steroidal sex hormones in sodium and water retention. They consider that the increased venous pressure of the legs, together with the diminished oncotic pressure of the plasma, may contribute somewhat to the retention of water. "The general tendency of normal pregnant women to retain sodium and water appears, however, to be best explained by the fact that they are constantly under the influence of enormous quantities of the steroid sex hormones. This effect is so predictable from the known physiologic properties of these substances that were the tendency to sodium and water retention not present, one would have to find an explanation for its absence." An interesting observation in this connec-

tion has been made by Friedlander and associates.[97] They found that estrogen administration was followed by sharp rises in the blood volume in both human subjects and in cats. This effect, however, was found only when the blood volume was initially low. Perhaps the constant influence of enormous quantities of the steroids during pregnancy could produce a like effect upon subjects with initially normal blood volumes. A role of these hormones in premenstrual edema is suggested by Thorn and Emerson[140] who review some aspects of the possible relation between the sex steroids and the sodium and water retention associated with premenstrual tension and edema.

The antidiuretic substances found in the urine of many toxemic and some normal subjects will not be reviewed here. The work of Gilman and Goodman[98] suggests that if a prerenal deviation of water occurs, there might be imposed upon the kidney the necessity for water reabsorption. If this be the case, the appearance of antidiuretic substances would be secondary. For reviews of subject, see Teel and Reid,[135], Krieger and Kilvington,[111] and Ham and Landis.[101]

In summary, the blood volume increase occurring in normal pregnancy accounts for the addition of an average of 2.9 pounds of water. The diminution in serum (plasma) proteins, averaging 1 gram per 100 ml., may account for an average increase of about 5.8 pounds of water in the interstitial spaces. The increased venous pressure of the legs favors water retention at this site. This last factor tends to be self-limited because the increasing volume of interstitial fluid exerts a back pressure (tissue turgor) which offsets the intravascular hydrostatic pressure. Also, fluid accumulated in the legs while the subject is up and about is largely mobilized and excreted during recumbency. The sex steroids also contribute a quantitatively unassessed part in sodium and water retention.

There have been but very few attempts to measure the water changes occurring in pregnancy. Chesley[74] has determined the thiocyanate-available (roughly extracellular) water in a large series of cases. Measurements were made in 67 cases in early pregnancy, and repeated at about 32 to 35 weeks. In another 375 normal cases, tests were made at 31 to 33 weeks and repeated at 35 to 37 weeks; in some cases measurements were again made at term. There seemed to be a gradually increasing rate of gain in the thiocyanate-available water. The total gain in pregnancy amounted to an average of 6.3 liters (13.85 pounds), of which 1.5 to 2.0 liters were thought to be in the conception product. The rest of the water presumably represented hydration of the maternal tissues, and totaled 9 to 10 pounds. Some of this water of hydration (perhaps about 4.5 pounds) has already been counted in the weight gain components discussed above; *i.e.*, 2.9 pounds in the increased blood volume, and an estimated 1.6 pounds in the new tissue of the uterus and breasts.

Chesley and Boog[76] made repeated measurements of the available water in 30 patients at delivery and in the puerperium. The total loss in available water, from just ante partum to the sixth week post partum averaged 6.1 liters (13.2 pounds), in good agreement with the estimated gain during pregnancy. The loss at delivery was accounted for in the fetus, placenta, amniotic fluid and blood loss. The major decrease, of 2.30 liters (5 pounds) occurred in the first six days of the puerperium.

Freyberg, Reekie and Folsome[96] determined the water balance by metabolic methods of Newburgh in 53 of the last 62 days of pregnancy

in a young primipara. The total water retention was 6.2 pounds, of which 2.05 pounds were attributed to protein and fat formation (is the stored nitrogen held as protein with the usual proportion of water? —see above). They subtract 2.2 pounds because the patient delivered in the middle of a salt and water excretion test; 0.54 pounds of water is assigned to the fetus, apparently as extracellular water. These corrections leave only 1.4 pounds for hydration of the maternal tissues. However, the interstitial fluid may have increased more than this, because the amniotic fluid was presumably decreasing (Beck), and the blood volume did decrease by 550 ml. Also the patient had a markedly positive sodium balance, gaining 17.12 grams of Na in this period. Unless stored in an osmotically inactive form (as in the bones), sodium is thought to be held extracellularly, and might be expected to withdraw some water from the cells in order to maintain osmotic equilibrium. In comparing this experiment with the measurements of thiocyanate-available water, it should be remembered that thiocyanate is thought to measure only the water outside of the cells (see below). It was suggested by Chesley and Annitto[75] that some cellular water perhaps does shift out to the interstitial compartment during pregnancy.

Hewitt and Van Liere[104] measured directly the water content of the liver, muscle and skin of guinea pigs. Neither the early or late, nor the early postpartum animals showed any significant difference from the controls. Childs and Eichelberger[79] determined the distribution and quantities of water and electrolytes in the skeletal muscle of 20 non-pregnant and 10 pregnant dogs. They found no water retention, no shift of water from one compartment to another, and no changes in the electrolytes during pregnancy. In a later paper, Eichelberger, Eisele and Wertzler[93] report similar determinations of water and electrolyte distribution in the skins of 3 pregnant dogs as compared with 10 non-pregnant controls. The average water content of the fat-free skins from the pregnant dogs was 752.1 Gm. per kg., as compared with an average of 708.3 Gm. per kg. in the controls. There was also a slight increase in the serum water of the pregnant dogs. Parhon, Cahane and Marza[123] found that pregnancy in the guinea pig increased the water content of blood, muscle, and liver. However, the average differences were slight.

TABLE X. THE RELATION OF MAXIMAL DIASTOLIC BLOOD PRESSURE READINGS AND OF EXCESSIVE WATER RETENTION TO THE SUBSEQUENT DEVELOPMENT OF PRE-ECLAMPSIA

MAXIMAL DIASTOLIC ON ANY OCCASION, MM. HG:	LESS THAN 65	66 TO 70	71 TO 75	76 TO 80	81 TO 85	86 TO 90	MORE THAN 90
Cases	70	182	154	398	139	171	77
Incidence of toxemia in all cases, per cent	0.0	0.5	2.6	5.0	9.4	18.1	32.5
Incidence of toxemia with normal water at time of test, per cent	0.0	0.6	1.6	2.2	6.3	11.5	12.2
Incidence of toxemia with excessive water at time of test, per cent	0.0	0.0	6.9	16.5	20.7	34.7	72.0

The negative sodium balances which Taylor and associates[133] found in the early puerperiums of their 3 human subjects (Table IX) are of about the magnitude to be expected from the readjustment of the

blood volumes alone. Hummel and associates[105] followed the mineral balance of a nursing multipara from the tenth day to the eighth week postpartum, and found a net *retention* of 22.27 Gm. of sodium in 43 days of lactation (where could this go?). From these 2 papers, then, there is not any evidence for the post-partum discharge of interstitial fluid gained during pregnancy. On the other hand, Crabtree[84] did find markedly negative water balances in the early puerperium. In the 8 cases observed for 6 days or more, the negative water balance ranged from 1,830 ml. (4.02 pounds) to 6,330 ml. (13.92 pounds), and averaged 4,440 ml. (9.8 pounds). These figures do not include water lost in milk, feces, lochia, and by transpiration. These last factors bulk considerably larger than does the preformed and metabolic water derived from the food, which factor was not considered by Crabtree.

These findings in guinea pigs and dogs raise the question as to the validity of the measurements of extracellular water by the thiocyanate method, at least in pregnancy. It is possible that during pregnancy the permeability of some cells may increase so as to admit thiocyanate. If this should happen, the thiocyanate-available water would include not only the extracellular water, but also the water of these cells. Alternatively, the pregnant woman may react differently from the guinea pigs and dogs, as indeed she does in her susceptibility to the pre-eclamptic syndrome. That she does so is strongly suggested by the clinical and physiologic observations detailed above, which point to water retention of about the degree indicated both by the thiocyanate tests, and by Crabtree's data on water losses after delivery. The work of Feldman and associates[94] indicates that species differences do exist. They found marked dilution of the blood in women and in rats during pregnancy, while the cow showed no such change.

In summarizing all of the components considered in the total weight gain of normal pregnancy, we have: Conception product 11.2 pounds, uterine growth 2.5 pounds, breast growth 3 pounds, protein retention not included in other factors about 4 pounds, blood volume increase 3.5 pounds, interstitial water increase not included in other factors about 4.5 pounds (? from thiocyanate measurements). These factors, which do not include fat gains, give a total, as a rough estimate, of 28.7 pounds which is 4.7 pounds more than the average weight gain (Table I). Elimination of the interstitial water gain would correct the difference, and might be rationalized by discounting the thiocyanate measurements or by considering that much of thiocyanate-available water had merely shifted out of the cells. Such water shifts seem to occur under the influence of the sex steroids.[80, 119, 145]

Toxic Pregnancy.—The water retention occurring in many cases of pre-eclampsia and eclampsia is too obvious to require discussion. Such edema formation frequently precedes hypertension and other signs of toxemia, and it is this which the clinician is looking for in his routine weighings of obstetric patients.

The cause of edema formation in incipient pre-eclampsia is unknown. Of the factors considered above in relation to water retention, none can be directly incriminated as the primary cause. 1. The venous pressure seems to be in the range of values found in the nonpregnant and normally pregnant subjects (see McLennan[116] for review). 2. The oncotic pressure of the plasma is perhaps a little lower in toxemia than in nor-

mal pregnancy (Table VIII), but most investigators have not regularly found decreases marked enough to account for the palpable edema (see Dieckmann and Kramer[88] for review). 3. The oncotic pressure of the interstitial fluids is not unduly increased in toxemia. The few determinations of the protein content of edema fluid from toxemic patients have shown concentrations of less than 0.4 Gm. per 100 milliliters[68, 87, 103, 112, 122]. 4. Changes in capillary permeability are largely unassessed, but cannot be gross as indicated by the low protein content of the edema fluid. McLennan[117] found that in edematous toxic patients the rate of filtration from the arm capillaries was less than in normal pregnancy. This, he explains, is probably attributable to the increased interstitial hydrostatic pressure (tissue turgor increased by edema) which opposes filtration. At least, these experiments seem to show that any increase in capillary pressure, decrease in oncotic pressure, and/or increase in capillary permeability are offset by opposing factors. 5. The sodium retention is increased, and in severe toxemia, the urine may be almost sodium-free.[67, 86, 88] However, this is merely another way of saying that edema is forming. 6. The blood and urine levels of the steroidal hormones are usually diminished in pre-eclampsia.[129, 131] Taylor has suggested, as an admitted speculation, that such diminution may mean an increased utilization which conceivably could increase the sodium and water retention. 7. Dieckmann[88] has considered a renal factor in the sodium retention and edema formation—"the renal function is altered if not actually temporarily impaired." Taylor, Warner and Welsh[133] point out that the measurements of renal blood flow and glomerular filtration[78, 83, 90, 110, 134] indicate no disturbance in renal function even in severe toxemia with marked hypertension. Perhaps the steroidal sex hormones act on the renal tubules to increase the reabsorption of sodium from the glomerular filtrate, as do the adrenal cortical steroids.[102]

Of the various components of weight gain in pregnancy, the one factor obviously related to the development of pre-eclampsia is water retention, and whatever value weight-taking may have in the detection of incipient toxemia probably depends upon the correlation between rapid weight gain and edema formation. It is, then, desirable to measure the water content or change in pregnant patients. There is available no generally practicable method for the determination of total body water. However, the extracellular water can be measured roughly by the use of thiocyanate[85, 114] (also by sucrose,[114] sulfate,[114] radioactive sodium or chloride,[109, 144] bromide,[142] or iodide[142]). Practically, this measurement is probably the more valuable, since most edema is largely extracellular.

Chesley and Chesley[11, 77] determined the thiocyanate-available (roughly extracellular) water in 1,388 patients in the last 10 weeks of pregnancy. At the time of the test, these patients manifested no sign of toxemia. The incidence of subsequent pre-eclampsia in 1,110 patients with normal proportions of available water, *at the time of the test,* was 3.9 per cent. Many of these toxic patients might have been detected had the test been done a second time, since the average time from the normal finding to the appearance of hypertension was six weeks. In 278 patients, (about 20 per cent of the series), having abnormally high proportions of available water, the incidence of the subsequently developing pre-eclamptic syndrome was 22.8 per cent. As done, the test picked out 59 per cent of the future pre-eclamptics (and missed 41 per cent). The test was not very specific in that 77 per cent of the patients selected as potential toxemias did not develop pre-eclampsia.

There were several factors which seemed to predispose to the development of toxemia in the patients with abnormal water retention. The incidence of pre-eclampsia in these patients increased with: 1. Lower serum proteins; 2. greater degree of water retention; 3. longer duration of water retention; 4. greater body weight; 5. higher maximal blood pressure (in upward spikes) occurring at any time, especially at the first clinic visit; 6. history of toxemia in a previous pregnancy.

The test was of little utility in about one-fourth of all patients, since the incidence of excessive water and especially of toxemia was low in patients whose blood pressure had never exceeded 110/70.

The importance of the maximal diastolic blood pressure, as observed at the time of single upward spikes, deserves special mention. Of the normal pregnancies, without regard to water measurements, 73 per cent of patients never showed on any occasion a diastolic pressure as high as 80 mm. Hg. Of the toxic pregnancies, 73 per cent of patients did show diastolic pressures of 80 mm. Hg or more on at least one occasion. Correlating the maximal diastolic pressure readings with the results of the available water measurements enables one to pick out different groups of patients in whom toxemia is highly unlikely to appear, and other groups in whom the toxemia incidence will exceed 70 per cent. This correlation is offered in Table X.

In summary, the causes of edema in pre-eclampsia are unknown. The formation of such edema can be detected early by the measurement of thiocyanate-available water, and many cases of toxemia can thus be picked out in their incipiency.

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Correspondence

Manual Dilatation of the Cervix Under Caudal Anesthesia

To the Editor:

In the May issue of the JOURNAL appeared a report by Rosenfeld on five cases of manual dilatation of the cervix under spinal anesthesia and in the August issue there was a comment on this subject by Kassebohm and Schreiber. Like the latter authors, I tried to dilate the cervix under spinal anesthesia but failed to carry out my purpose with the ease claimed for this procedure first by Delmas in 1928, and more recently by others. Doctors Kassebohm and Schreiber referred to the editorial comment I made on Koster and Perrotta's article concerning the Delmas' procedure in the *1943 Year Book of Obstetrics and Gynecology.* Unfortunately, some physicians are now resorting to the Delmas' method of accouchement forcé and in the hope of dissuading some unskilled ones from attempting to carry out this procedure, may I call attention to my comment which is as follows:

"One of the most pernicious attempts to revive accouchement forcé was made by Koster and Perrotta (Exper. Med. & Surg. **1**: 143, May, 1943). Koster is a general surgeon, and therefore he is not expected to know much, if anything about obstetrics. I don't know what specialty if any Perrotta practices because I could not find either Koster's or Perrotta's name in the 1942 Directory of Medical Specialists. These men report a series of 39 cases in which they took pregnant women before term, gave them a spinal anesthetic and then 'stretched the cervix in various directions until successively two, three and finally four fingers are introduced into it.' After rupturing the membranes, they delivered the baby by forceps or version and extraction.

"In 1928, Delmas of Montpelier, France, advocated exactly the same procedure. The toll of deaths of mothers and babies which followed this monstrous treatment led to abandonment of it. Ostreil (Zentralb. f. Gynäk. **58**: 325, Feb. 10, 1934), analyzed a series of 120 of these rapid dilatations under spinal anesthesia performed by 30 French obstetricians who reported their results. There were 24 cases of deep cervical lacerations, 2 of complete laceration of the perineum, 2 of ruptured uterus; in 3 cases dilatation could not be carried out, and in 2 cases vaginal cesarean section had to be done. In this series of 120 cases there were 8 maternal deaths and 9 fetal deaths!!

"The majority of obstetricians agree that spinal anesthesia is the most dangerous anesthetic for pregnant women. Koster and Perrotta claim otherwise, but that is their opinion and they are entitled to it. However, with complete and utter disregard for human welfare, these authors say: "Regarding the objection to operative delivery, it must be conceded that it is the price for electively terminating a pregnancy without labor or pain." This is a remarkable attitude for a physician to take. I feel certain that if the dangers of the Delmas' procedure were pointed out to pregnant women, Koster and Perrotta would have very few patients on whose cervices they would exercise their fingers."

J. P. GREENHILL, M.D.

CHICAGO, ILL.

SEPTEMBER 7, 1944.

To the Editor:

In the August number of the JOURNAL, page 281, Doctors Kassebohm and Schreiber make a passionate attack on the procedure of accouchment forcé. I am just as much opposed to unindicated and indiscriminate accouchment forcé as they are, and in a paper recently read by me before the Obstetrical and Gynecological section of the New York Academy of Medicine entitled "The Place of Rapid Vaginal Delivery Under Spinal Anesthesia," I stated that if this procedure should come to be extensively utilized by general practitioners and young specialists that both the maternal and fetal mortalities and morbidities would rise precipitously. I further stated that if one wishes to retrogress and go back to accouchment forcé, he can perform that procedure almost as well under general as under spinal anesthesia.

They question my statement that under spinal anesthesia, the musculature of the cervix relaxes while the musculature of the corpus contracts. They ask are there muscles in the cervix at term or are there merely some muscle fibers? They also ask why should muscle fibers in one portion of an organ relax when the tonus of the fibers in another portion of the same organ increases.

With reference to the presence of muscle fibers in the nonpregnant cervix, authorities including Stahr, Cunningham and Piersol all agree that the cervix contains muscle tissue, and moreover, that the stratification of the muscle tissue in the cervix is more pronounced than in the corpus.

During pregnancy, most authors of texts are agreed that the cervix contains muscles, though the hyperplasia noted in the corpus is absent. Beck states that the muscle fibers in the cervix diminish in number, but those that remain undergo hypertrophy. Otto H. Schwarz writing in Curtis' system says that the cervix increases in size during pregnancy as a result of the hypertrophy of the muscle fibers just as does the body of the uterus. All authors are in agreement that there is a marked increase in the amount of fibrous, elastic and vascular tissues. So much so that the cervix is practically an erectile organ during pregnancy.

It is hard to conceive that all the above described muscle tissue disappears or is rendered functionless at term or during parturition.

As to nerve innervation, it is well known that systems and organs containing smooth muscle are automatic and that they function despite severance of all extrinsic nerves. Nevertheless, drugs and stimuli acting on the extrinsic nerves influence and largely determine the reactions of these structures.

Pharmacologic and physiologic literature is replete with instances where a given drug will act as a pressor in one section of the intestine and as an inhibitor in another segment. For example, Melville and Stehle have demonstrated that the oxytocic principle of pituitary extract when given to dogs leaves the colon unaffected, causes relaxation of the circular muscle in the small intestine and produces contraction of the longitudinal muscle. None of the contents of the small bowel passes through the ileocecal valve.

Newton, after demonstrating the power of the cervix to contract, showed that the corpus and cervix exhibited not only opposite reactions to adrenalin but that the cervix proved quite insensitive to pitocin. He also showed in rat uteri that the muscles of the horns do not uniformly respond to pitocin.

In the same manner we know that nerves, with wide distribution, carry pressor impulses to some tissues and organs and inhibitory impulses to others. Reynolds in his text *Physiology of the Uterus*, states that aside from the region of the cervix the musculature of the uterus is devoid of a ganglionic nervous system. I quote this passage to show that some difference exists between the nerve patterns of the cervix and the corpus.

Unfortunately, we are ignorant of many of the basic facts underlying the functions of the uterine nerves, but our inability to explain these functions in no way alters them nor does it change their effects.

As to some of the other questions raised by Doctors Kassebohm and Schreiber—"Is it possible to efface the cervix manually?" I don't know as I never tried it at term. I have never attempted manual dilatation unless the cervix was effaced. I did try on one occasion to dilate a cervix manually in early pregnancy (therapeutic abortion) under spinal anesthesia but did not succeed.

When it comes to dilatation of the cervix, certainly the cervix can be dilated manually if by dilatation one means to spread out or make wider.

"Are many of the cervices lacerated in the performance of manual dilatation?" Yes, but so are they by other methods of delivery. It is well known that a great many lacerations of the cervix occur without most attendants either seeking or being aware of their presence.

"Does the cervix or the internal os become more pliable after spinal anesthesia?" Definitely yes. It makes no practical difference whether this pliability is due to the inhibition of the cervical muscles or changes in the cervical vascular pattern, for admittedly either of these effects would have to be mediated through the nervous system. Cervices that I was unable to dilate under local and paracervical anesthesia, I was readily able to dilate under spinal. I admit and from personal experience know that manual dilatation can be performed under other forms of anesthesia.

"Do the corporeal muscles contract under spinal anesthesia?" From experience with both vaginal and abdominal delivery under spinal anesthesia, my answer is a categorical yes. The uterine contractions do not cease while the patient is under the influence of the anesthetic. In over one-half of the patients whom I desired to deliver by podalic version, I had to resort to forceps, because the corpus was so tightly contracted proper entrance of the hand into the uterine cavity could not be effected. In two such instances, ether anesthesia was superimposed on the spinal and version was then performed with ease.

I prefer spinal to general anesthesia because with the former the blood loss is greatly diminished, the child cries spontaneously so that resuscitation is rarely required, shock occurs less often and cervical repair is facilitated because the field is so much drier than under general anesthesia.

I believe that the procedure has a very limited field and the indications are few, but when the proper indications are present and if the operation is performed by a competent obstetrician it can save many an infant's life and many hours of maternal travail. It is not a pain-relieving method in the sense that caudal anesthesia is, and it should not be so employed.

In conclusion, I do not believe that truth can be successfully scotched. Let us rather thoroughly discuss and compare experiences rather than bury a method that admittedly is useful in trained hands. It would be just as logical to "forget about" forceps and versions because incompetents might attempt these beautiful and lifesaving procedures. Let us rather train our doctors so that they may be competent obstetricians and at the same time educate the public so that they demand expert service.

SAMUEL S. ROSENFELD, M.D.

NEW YORK, N. Y.
SEPT. 5, 1944

Society Transactions

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF MAY 5, 1944

The following papers were presented:

Hemorrhage as the Most Important Cause of Maternal Death in Brooklyn in 1943. Charles A. Gordon, M.D., (For original article, see page 557.)

Personal Recollections of Dr. Joseph B. DeLee. J. P. Greenhill, M.D.

Item

American Board of Obstetrics and Gynecology, Inc.

A number of changes in Board regulations and requirements were put into effect at the Board's last annual meeting. These were designed to aid civilians as well as candidates in the Service. Among these is the waiver, temporarily, of the A.M.A. requirement for men in the Army or Navy, especially for those who proceeded directly or almost so from hospital services into Army or Navy Service, upon a statement of intention to join promptly upon return to civilian practice. At this meeting the Board decided also to accept a period of nine months as an academic year in satisfying our requirement for certain years of training. This is only for the duration and even men who are not eligible for Military Service but who are nevertheless in hospitals where the accelerated program is in effect have been allowed to submit to us this short-time period of training in lieu of our previous requirements.

Beginning with the next written examination, which is scheduled to be held the first Saturday afternoon in February, 1945, this Board will limit the written examination to a maximum period of three hours and in submitting case records at this time, all obstetric reports which do not include measurements either by calipers and, as indicated, by acceptable x-ray pelvimetry, will be considered incomplete.

Prospective applicants or candidates in Military Service are urged to obtain from the Office of the Secretary a copy of the "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards" which will be supplied upon request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the Offices of the Surgeons-General, having been recommended to the Services in a circular letter, No. 76, from the War Department Army Service Forces, and referred to as the Medical Officer's Service Record. These will enable prospective applicants and candidates to keep an accurate record of work done while in Military Service and should be submitted with the candidate's application, so that the Credentials Committee may have this information available in reviewing the application.

Applications and BULLETIN of detailed information regarding the Board requirements will be sent upon request to the Secretary's Office, 1015 Highland Building, Pittsburgh, 6, Pennsylvania. Applications must be in the Office of the Secretary by November 15, 1944, ninety days in advance of the examination date. The time and place of the Spring 1945 (Part II) examination will be announced later.

PAUL TITUS, M.D.

1015 HIGHLAND BUILDING,
PITTSBURGH, 6, PA.

The following physicians have recently completed our requirements and have now been certified by the American Board of Obstetrics and Gynecology:

Burkons, Harold F. M.D., 1170 Everglades Concourse, Miami Beach, Fla.

Kantor, Herman I. M.D., MDETS, Billings General Hospital, Fort Benjamin Harrison, Ind.

Stern, Alfred, M.D., 355 30th Street, Oakland, Calif.

Wolff, Frederick Siegfried, Captain (MC), MDETS, Fort Snelling, Minneapolis, Minn.

PAUL TITUS, M.D.

Secretary.

Necrology

FREDERICK CLARK HOLDEN, M.D., D.P.H. (Hon.), Director of Gynecology at the Jersey City Medical Center and Professor Emeritus of Obstetrics and Gynecology at the New York University Medical School, past President of the American Gynecological Society, the New York Obstetrical Society, and consultant in several hospitals, long a resident of New York City, died suddenly at Prout's Neck, Maine, on August 27, in the 75th year of his age.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President,* Edward A. Schumann, Philadelphia, Pa. *Secretary,* Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* Lewis F. Smead, Toledo, Ohio. *Secretary,* James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.

Central Association of Obstetricians and Gynecologists. (1929) *President,* John H. Moore, Grand Forks, N. D. *Secretary-Treasurer,* W. F. Mengert, Dallas, Tex. Annual meeting not announced.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President* Oren Moore, Charlotte, N. C. *Secretary,* T. J. Williams, University, Va. Annual meeting cancelled.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Philip F. Williams, Philadelphia, Pa. *Secretary,* William Mengert, 2211 Oak Lawn Ave., Dallax Tex. Next meeting, New York City, June, 1945.

New York Obstetrical Society. (1863) *President,* W. E. Studdiford. *Secretary,* R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. (1868) *President,* Charles A. Behney *Secretary,* John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President,* William J. Dieckmann. *Secretary,* Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President,* James P. McManus. *Secretary,* William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President,* Lawrence Wharton. *Secretary-Treasurer,* John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. *President,* Edward Friedman. *Secretary,* Carroll J. Fairo, Cincinnati, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Layman A. Gray. *Secretary,* E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Howard Stearns. *Secretary,* William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* H. A. Power. *Secretary,* Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.

Obstetrical Society of Boston. (1861) *President,* Thos. Almy, Fall River, Mass. *Secretary,* Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

New England Obstetrical and Gynecological Society. (1929) *President,* Roy J. Hefferman, Brookline, Mass. *Secretary,* Fred J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* T. Floyd Bell. *Secretary-Treasurer,* William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.

Washington Gynecological Society. (1933) *President,* James R. Costello. *Secretary,* J. Keith Cromer, 1835 Eye St., N.W., Washington, D. C. Fourth Saturday, October to May.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* E. L. Zander. *Secretary,* R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.

St. Louis Gynecological Society. (1924) *President,* S. A. Weintraub. *Secretary,* Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President,* R. Glenn Craig. *Secretary,* D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* T. F. Bunkley. *Secretary,* J. McIver, 714 Medical Arts Bldg., Dallas, Tex.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* Norman F. Miller. *Secretary,* Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Obstetric Society of Syracuse Hospitals. (1938) *President,* Edward C. Hughes. *Secretary,* Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.

Alabama Association of Obstetricians and Gynecologists. *President,* J. M. Weldon, Mobile, Ala. *Secretary,* Eva F. Dodge, Montgomery, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* R. Philip Smith. *Secretary,* Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings held on third Wednesday of each month.

Denver Obstetrical and Gynecological Society. (1942) *Secretary,* Emmett A. Mechler, 1612 Tremont St., Denver, Colo. Suspended during war.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* Roland S. Cron. *Secretary,* Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* Geo. D. Huff. *Secretary,* Frank Russell, 233 A St., San Diego, Calif. Meetings held on the last Wednesday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Ralph E. Leigh, Grand Forks. *Secretary,* G. Wilson Hunter, 807 Broadway, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* A. L. Carson, Jr. *Secretary,* L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.